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## Original Communications

### THE INTERRELATIONSHIP OF DISEASE OF THE CORONARY ARTERIES AND GALL BLADDER

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FOR half a century, at least, clinicians have insisted that more than an accidental association exists between disease of the heart and of the gall bladder. Three reasons, principally, have been advanced as proof: (1) Anginal pain, and myocardial incompetence, signalized by heart failure, will undergo improvement and disappear upon removing a diseased gall bladder,<sup>1</sup> (2) electrocardiographic abnormalities which are characteristic of the myocardial damage induced by coronary artery disease may disappear after extirpation of a diseased gall bladder,<sup>1</sup> and (3) the concurrence of gall bladder disease and cardiac affections, notably coronary artery disease, is apparently much greater than one would expect, even when due allowance is made for the natural or predictable incidence of the disease in question at various ages.

Although they are suggestive and provocative, these arguments fall short of being wholly convincing; indeed, some of the earliest observers reached their conclusions on the basis of rather flimsy or erroneous suppositions. Nevertheless, the concept of an interrelationship between dysfunction of the gall bladder (or other parts of the bile duct system) and the coronary circulation (or other parts of the cardiovascular apparatus, e.g., the myocardium) will not down; and a similar interdependence may hold for other supradiaphragmatic and infradiaphragmatic organs. We propose, therefore, to discuss clinical, as well as anatomic and physiologic, evidence which may be marshalled to support the hypothesis of a common mechanism. This evidence is furnished mainly (a) by an analysis of the general behavior, the mass excitation, of the autonomic nervous system as a whole, (b) by precise evaluation of the localization and projection of pain, and (c) by recognizing the function of commonly shared afferent pathways which are capable of transmitting abnormally registered pain from one organ to another.<sup>2</sup>

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To avoid repetition, clinical reports are omitted, except of the concurrence, in two cases, of disease of the coronary and bile duct systems.

#### I. CLINICAL ASPECTS

1. *Incidence.*—Coronary artery occlusion in association with disease of the gall bladder appears to be on the increase. This has been attributed chiefly to improved methods of diagnosis and to an increase in the number of persons who survive until the fifth, sixth, and seventh decades; the latter factor raises the absolute number of coronary, as well as gall bladder, victims. That progress has been made in diagnosing gall bladder and coronary artery disease cannot be denied, and it is safe to assume that the total number of victims of both disorders has increased since the span of life has been lengthened. Certainly the decades between 40 and 70 years include many patients with coronary and gall bladder disease. In still older people, the very aged, a decreescent state of the tributaries of the heart is frequently found, but many in this group will have very mild or no symptoms at all, and therefore are not to be classified strictly as patients with coronary disease. However, it is to the point that these persons may develop pronounced anginal attacks when, as often happens, gall bladder disease supervenes.

Gall bladder disease in the very old is more frequent than is generally suspected. In homes and institutions for the aged, disorders of the gall bladder in both sexes are not at all rare. The onset may be sudden or slow and insidious, or it may be manifested by painless jaundice. Mild or moderate tenderness in the gall bladder region is sometimes the sole indication. In older persons, as well as in younger, the chronic "grumbling" gall bladder, even if silent for long periods, may continue to give rise to further paroxysms, and this possibility seems to be enhanced when the cardiovascular apparatus becomes affected.

2. *Diagnosis.*—Because the local signs, notably pain and its radiation, are quite characteristic in each disorder, disease of the gall bladder is distinguished without difficulty, as a rule, from disease of the coronary artery system. On the other hand, the clinical aspects of the general reaction may provide no distinguishing clues because disease of the gall bladder or coronary system may induce a common, generalized, autonomic response.

(a) *The General (Autonomic) Reaction.*<sup>2a, 8</sup>—This consists of sympathetic (adrenergic) and parasympathetic (cholinergic) manifestations. To the former belong shock, cardiovascular collapse with attendant blood pressure changes, prostration, psychogenic disturbances such as marked anxiety, and glycosuria. The cholinergic features, which are more conspicuous with infradiaphragmatic disease, frequently are manifested by bradycardia and other changes in cardiac conduction, meteorism,

undue salivation, and vertigo. Fever, polyuria, disturbance of the sleep-waking mechanism, and leucocytosis are also central autonomic derangements, but they cannot be labelled as sympathetic or parasympathetic.

Any or all of these autonomic reactions are known to accompany sudden involvement of the gall bladder or coronary arteries. As a rule, a vigorous autonomic response is associated with a sudden, explosive process in the gall bladder or coronary artery system, and milder and less extensive autonomic manifestations accompany or follow chronic, "smoldering" diseases of these organs. Yet, in these divergent states, the mechanism and pathways for pain may be quite similar, and, as we shall see, even identical.

(b) *Pain*, especially its reference, is perhaps the single most important guide in differential diagnosis. It is well, however, to re-emphasize that pain need not be the sole or even the chief evidence of either coronary artery occlusion or gall bladder disease. However, when it is present, the pain often furnishes telltale evidence. This is so because each organ, as a rule, will reflect pain into a related dermatomic area.

Difficulties in diagnosis arise when the pain is referred to distant dermatomes which are not directly related to the organ primarily involved. Thus, with an attack of acute cholecystitis the pain may be referred into the cardiac zone of reference, namely, the left pectoral and forearm region; or the pain of acute coronary occlusion may be referred into the right flank. Furthermore, pain which is referred into the right posterior shoulder region may be thought to originate in the gall bladder, and really be due to pericarditis associated with coronary disease.

Acute gall bladder disease (cholecystitis, empyema), acute pancreatitis, sudden perforation of the stomach, duodenum or intestine, and acute generalized peritonitis are abrupt, explosive conditions characterized by pain and general manifestations which again suggest a mass excitation of the entire autonomic system. Bowel obstruction or mechanical obstruction of any hollow structure, such as the ureter or bile duct, extensive infarction of an organ, or thrombosis of large abdominal or thoracic vessels (including the pulmonary), or dissecting aneurysm of the aorta induce pain and associated features which sometimes closely simulate the intense anginal attack of acute coronary thrombosis.\*

Although it is a rare occurrence, the pelvic organs, male or female, may engender pain that finds its way to the cardiac region; the reverse of this is also true. Abdominal viscera act in a similar way, and the organs closest to the diaphragm cause the most pronounced effects. For example, no other condition more closely simulates acute coronary

\*Gilbert and his associates<sup>2c, 3</sup> claim that afferent impulses from upper abdominal viscera (gall bladder, stomach) may produce reflex vagal coronary artery constriction, and thus cause anginal pain. It is not clear, however, whether such a reflex will account for all instances of gall bladder or stomach pain referred into the cardiac dermatomes. The principle of "over-lapping" afferent impulses, it seems to me, cannot be excluded (see II).

thrombosis than esophageal herniation. Upper abdominal organs possess a double and full innervation (sympathetic and parasympathetic), and perhaps also a more diffusely developed system of visceral afferent fibers. Organs lower in the celomic cavity are not as well developed in this respect, and this may account for the fact that they rarely act as sources of explosive attacks.

*Electrocardiographic evidence*, also, may sometimes be quite misleading, in at least one of two ways: acute coronary occlusion may fail to cause electrocardiographic changes in the ensuing week or two, or not at all; or an acute gall bladder attack may be accompanied by electrocardiographic changes which are suggestive of myocardial infarction.

3. *Clinical Groups*.—In a general way, the clinical material which exemplifies the interrelationship between gall bladder and coronary disease falls into three groups.

Group 1 consists of patients who develop acute disease of the gall bladder which simulates acute coronary occlusion, or vice versa. In both cases the general constitutional (autonomic) reaction is likely to be violent and widespread, and practically identical. Differential diagnosis on the basis of the common general reaction therefore will not be possible. Nor will the usual guide with respect to the site and reference of pain be available, for the pain may be transmitted by accessory afferent pathways.

Group 2 comprises patients who develop acute coronary occlusion and gall bladder disease almost simultaneously, or within a few hours or days of each other. This problem is not one of simulation or overflow of manifestations from the organ involved to the other viscus. Two organs are acutely implicated, giving rise to common signs and symptoms. Although it is decidedly less frequent than that of Group 1, this set of circumstances is not rare. Summaries of two illustrative cases are cited.

CASE 1.—L. M., 68 years old, who was in excellent health, was suddenly seized, soon after an evening meal, with agonizing upper epigastric and precordial pain. Shock and cyanosis came on at once, and the cyanosis persisted even when oxygen was administered. During the subsequent four days he had recurrent attacks of severe precordial pain, associated with bloody, frothy sputum; there were also attacks of peripheral, as well as cardiac, collapse, and of transient auricular fibrillation. Despite negative electrocardiographic tracings on the 2nd, 8th, and 16th days, the possibility of coronary occlusion could not be excluded. Five days after the onset of the illness he developed mild jaundice which was at first attributed to pulmonary changes attendant upon infarction. The jaundice steadily deepened, and a tender gall bladder mass became palpable. Fever and leucocytosis continued, and the temperature ranged from 102° to 103° on the tenth day. Surgical opinion held that the primary disease was either acute pancreatitis or acute cholecystitis with cholangitis. Laparotomy revealed acute cholecystitis. The patient succumbed to an attack of heart failure on the following day. Autopsy disclosed recent cholecystitis, extensive recent myocardial infarction, and recent thrombosis high up in the left descending coronary artery.

CASE 2.—H. O., 56 years old, was suddenly seized with intense precordial pain, shock, and fever. Acute coronary occlusion was diagnosed. On the following day, a "suggestive" chill and a temperature of 105° developed; the liver suddenly enlarged until it extended about 2 finger breadths below the free costal margin, and the gall bladder became readily palpable and very tender. Operation was postponed because of the serious cardiac condition. The gall bladder disease subsided gradually, but the features associated with myocardial infarction persisted for about four months. The electrocardiogram ten weeks after the onset of the attack showed a sharply inverted T<sub>4</sub>.

Group 3 comprises patients with chronic disease of both organs or systems. The autonomic reactions with respect to both organs may be almost identical, but the clinical manifestations of the somatic alteration in the organ (or system) may well serve as a reliable basis for differential diagnosis. For example, the train of clinical events in slowly developing myocardial infarction is generally unmistakable from that of cholelithiasis or other causes of obstructive jaundice. However, the respective and characteristic general clinical manifestations may be lacking or minimal. Confusion in diagnosis may then arise, particularly if pain is referred by "overlapping" afferent pathways into atypical dermatomic areas.

Closely allied are certain cases in which there are chronic recurrent manifestations with pain in many organs and related districts of the body. These sufferers are frequently brushed aside as neurotic, or become the unfortunate subjects of repeated and futile operations. They are persons, we strongly suspect, whose afferent conducting pathways are diffuse, thus rendering possible the projection of pain from one viscus into the dermatomic areas of multiple organs.

## II. THE MECHANISMS AND ROUTES OF VISCERAL REFERRED PAIN

1. *The Dual System of Pathways Commonly Involved.*—Two independent nerve pathways cooperate in the propagation of referred visceral pain. Impulses of pain, for example, which originate in the heart, coronary vessels, or aorta are transmitted into the upper left thoracic spinal cord segments (T 1 to 4) by corresponding afferent (sympathetic) visceral fibers. At these levels, afferent somatic nerves (the upper intercostals) are brought into action, and these, together with the visceral fibers, function to refer pain into complementary related dermatomes. As is well known, these dermatomes consist of the left infra-clavicular or pectoral region and the inner aspect of the left arm. The reference of pain from organs other than the heart into related dermatomes is accomplished by a similar cofunction of visceral and somatic afferent neurons.

In most persons the visceral afferent neurons converge predominantly upon a limited group of dorsal roots at a particular cord level, and thus come into relation with a corresponding restricted group of afferent somatic fibers. In the case of the heart, the preponderance and convergence of entry is at the levels T 1 to 4 on the left side. For

the gall bladder the levels are approximately T 8 and 9 and perhaps 7, according to Head;<sup>4</sup> T 9 and 10, according to Kappis<sup>5</sup> and L  wen,<sup>6</sup> and on the right side. This rather well-defined concentration of afferent visceral fibers makes it possible for each organ to refer pain which is engendered in it to the related surface zones, and this enables the physician in the majority of cases to recognize the site of visceral pain according to the complementary dermatomes that are implicated. More

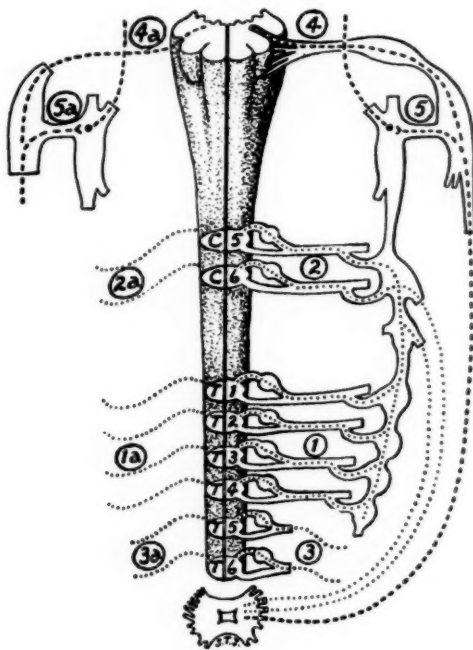


Fig. 1.—(From *Angina Pectoris* by H. R. Miller, Grune and Stratton, New York, 1942. Reprinted by permission of the publishers.) This is a schema of groups of afferent fibers capable of transmitting referred anginal pain. (1) Represents the usual, well-recognized, sinistral group entering the Th 1 to 4 cord segments through corresponding white rami; (1a) is a similar dextral group much less frequently involved. (2) Represents upper left cervical fibers going from upper cervical ganglia to corresponding cervical cord segments; (2a) similar dextral fibers. (3) Represents lower thoracic fibers going from the lower thoracic ganglia to corresponding cord levels; (3a) dextral fibers. (4) Represents the pathway of cardiac afferent fibers in the left vagus destined for the medulla; (4a) a similar pathway on the opposite right side. (5) Represents the pathway of vagal cardiac afferent fibers which ends in the superior cervical sympathetic ganglion; (5a) a similar pathway on the opposite right side. (6) Not included in the drawing is the posterior group of rami connecting the upper thoracic sympathetic chain to the cardio-aortic plexuses. (7) Also not included are the sympathetic fibers from the vertebral plexus, entering the cervical plexus and sending communications to the ansa of Vieussens. The vertebral plexus is generally not accepted as an afferent pathway for cardio-aortic pain.

recently, Ashkenaz<sup>7</sup> has demonstrated that the gall bladder is connected to the neuraxis by afferent pathways which are far more numerous than we were formerly led to believe, namely, from T 1 to 12, and even lower, on the right side, and from about T 5 to 10 on the left side. The entry of afferent impulses from the gall bladder, which is usually restricted to T 8 to 10 on the right, may therefore readily include many more segmental levels on both sides.

2. *The Participation of Accessory Visceral Afferent Fibers.*—Occasionally, the heart or gall bladder refers pain into an uncommon dermatomic territory. In such cases accessory afferent fibers transmit the impulses of pain into levels of the cord other than those commonly involved—in

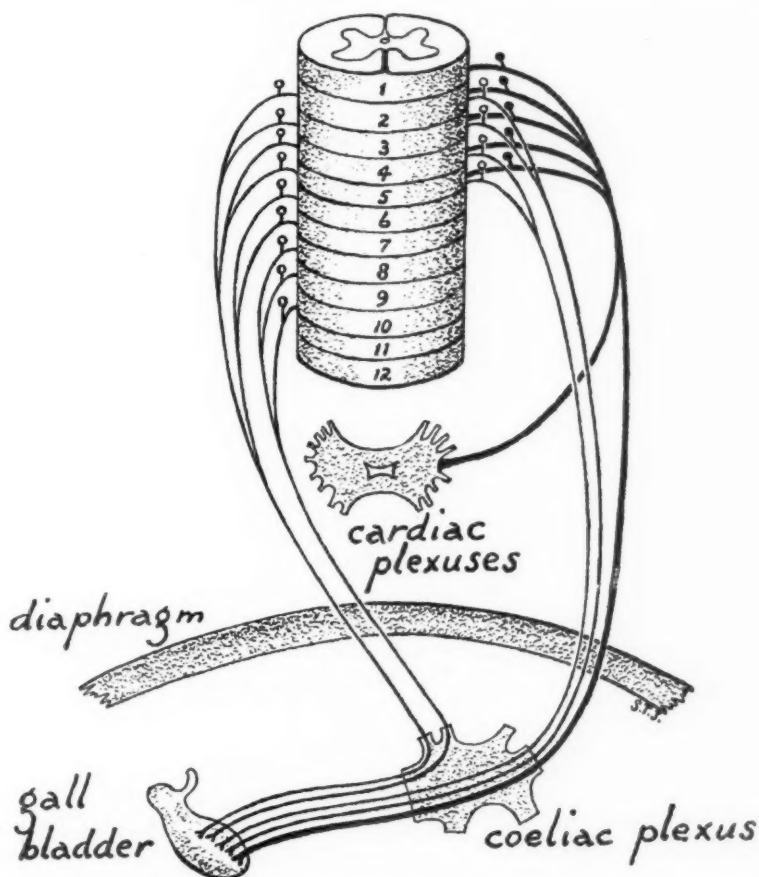


Fig. 2.—The pathways for referred pain from the gall bladder into the cardiac territory. (From *Angina Pectoris* by H. R. Miller, Grune and Stratton, New York, 1942. Reprinted by permission of the publishers.)

The gall bladder has many afferent fibers entering almost every level of the thoracic cord on the right side and a number of upper levels on the left side as well. The cardiac afferent fibers have their usual entry into the upper four thoracic segments of the left side. The radiations of gall bladder and heart disease are, therefore, as a rule, distinctly apart and registered in characteristically different areas of the body. When gall bladder pain is referred into the cardiac territory, we may explain it, on the basis of an arrangement of fibers illustrated above. The predominance of entry of afferent fibers from the gall bladder is indicated as on the *left* side of the upper thoracic cord, the zone in which anginal referred pain is mediated. The same scheme would hold if the mediation were in dorsal ganglia or roots.

other words, outside the zone of the cord which receives the concentration, i.e., the bulk of fibers. Usually, the accessory fibers are too few or too diffuse to carry an appreciable quantity of pain impulses. In certain persons, however, one or more organs may lack a concentration of afferent visceral fibers for any sharply defined segmental zone of the cord.

The arrangement of afferent fibers with respect to any viscus, whether concentrated or diffuse, represents a fundamental anatomic pattern in each case. When this pattern lacks a preponderance of entry into the cord, or when, for some reason, the zone of concentration (the "bottle-neck" in the case of the heart innervation) is interrupted or destroyed, the burden of afferent conduction may be thrown upon the accessory

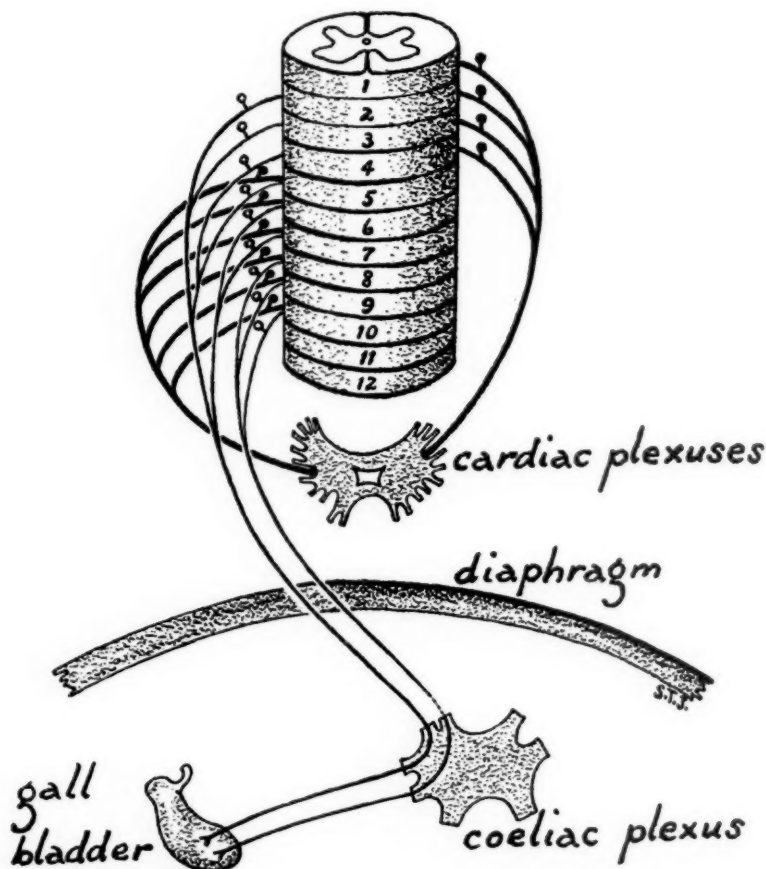


Fig. 3.—The pathways for referred anginal pain into the gall bladder region. (From *Angina Pectoris* by H. R. Miller, Grune and Stratton, New York, 1942. Reprinted by permission of the publishers.)

This drawing illustrates the arrangement of afferent fibers that would prevail in those cases when anginal pain is propagated into the gall bladder region.

The cardiac afferent fibers are drawn here as predominantly *dextral*, and overlapping the entry zone of the main group of afferent fibers from the gall bladder.

groups of fibers. Fig. 1 is a schema of the accessory groups which are concerned with cardiovascular pain, and illustrates the principle that transmission of pain from a viscus can take place by specially concentrated groups of fibers or by diffuse pathways.

This principle of an uncommonly prominent participation on the part of accessory visceral fibers may be invoked to explain the reference of

pain from one organ into the other. For example, when cardiac pain is referred into the dermatomes related to the gall bladder, the reference is by means of accessory fibers which leave the heart and go to cord levels that are concerned with the mediation of gall bladder pain. Conversely, a similar mechanism operates when gall bladder pain is referred into the dermatomic territory which is commonly the recipient of cardiac pain. Figs. 2 and 3 illustrate these mechanisms. A common mechanism accordingly underlies the reference.

#### CONCLUSIONS

The premise of an interrelationship between disease of the gall bladder and the coronary arterial system rests upon evidence that (1) a common general autonomic reaction is set off in each disorder, and that (2) a common mechanism and afferent pathways are brought into action when the referred pain of coronary occlusion simulates that of gall bladder and bile duct affections, or vice versa.

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## AURICULAR FLUTTER ASSOCIATED WITH BIZARRE QRST COMPLEXES

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**A**URICULAR flutter is a common and, for the most part, easily diagnosed condition. Clinically, a fast heart rate, with rapid auricular pulsations of the neck veins, serves to make the diagnosis. Electrocardiograms show the regular auricular waves, at a rate of about 300 per minute, which give the base line a characteristic "saw tooth" appearance.

When the auricular flutter, however, is accompanied by changes in the ventricular complexes, it is not as easily recognized in the electrocardiogram. During the past three years several electrocardiograms which showed very fast rates and bizarre wave forms have come to our attention. These were variously diagnosed as nodal rhythm with bundle branch block, ventricular tachycardia, auricular tachycardia, etc. In studying these tracings we have come to the conclusion that many of them are records of auricular flutter with a superimposed deformity of the QRST waves which obscures the auricular flutter waves.

In 1916, White and Stevens<sup>1</sup> reported a case of paroxysmal 1:1 auricular flutter in which, after a very few minutes, aberrant ventricular complexes developed, with subsequent return to normal rhythm. They thought that the aberrant ventricular complexes represented exhaustion of part of the conduction system. An interesting case of 2:1 auricular flutter was described by Cutts and Roberts,<sup>2</sup> in 1938. In this instance alternate ventricular beats showed a wide QRS complex of the left bundle branch block type. The rhythm eventually returned to normal, with normal ventricular complexes. Gupta and Sinha<sup>3</sup> have recorded a case of "auricular flutter with a paroxysmal ventricular tachycardia showing reversion to normal rhythm." From a study of their published tracings we feel that they are more likely examples of auricular flutter with interventricular block. Szekely<sup>4</sup> reports the case of a 43-year-old man who was suffering from attacks of tachycardia after posterior myocardial infarction. These electrocardiograms are difficult to analyze from the published data, but are very similar to some of the tracings included in this paper.

Recent texts on electrocardiography make little or no reference to auricular flutter associated with block of the ventricular conduction system. Graybiel and White<sup>5</sup> show two instances, but in each case the

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deformity of the ventricular complex is insufficient to obscure the flutter wave.

Because we feel that in many instances this type of electrocardiogram may be unrecognized, we are reporting the following cases which are illustrative of the condition.

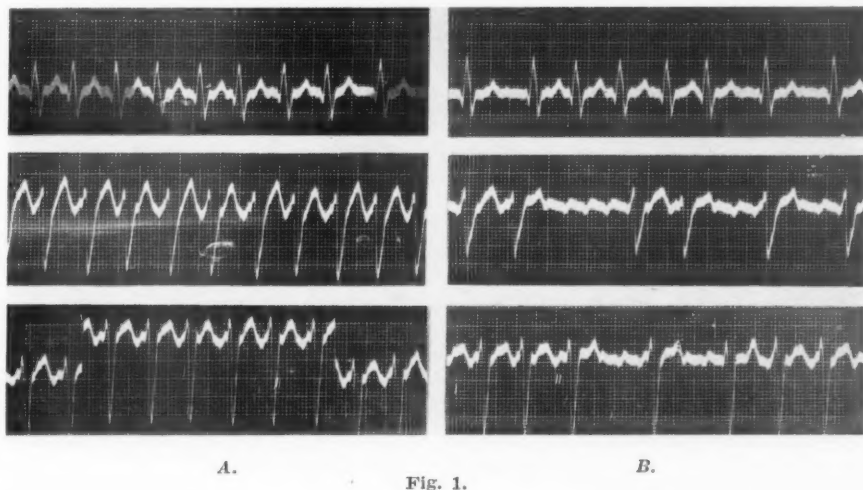


Fig. 1.

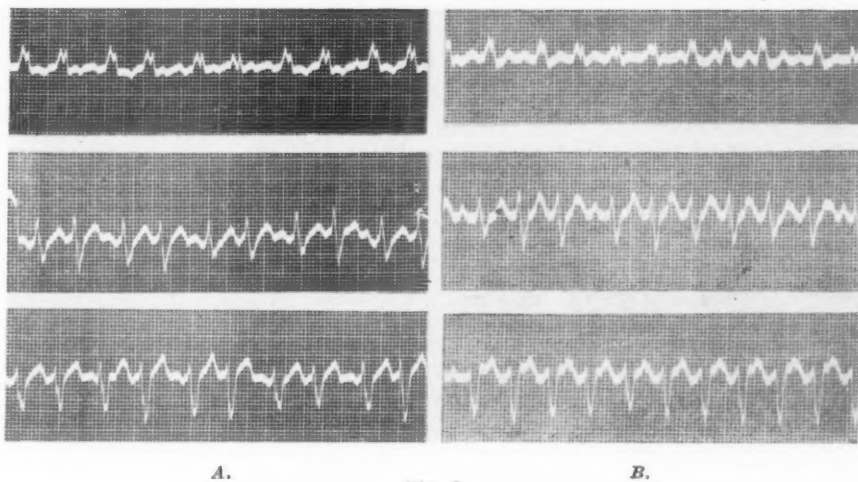


Fig. 2.

CASE 1.—J. L. This 65-year-old man was referred from another hospital for an electrocardiogram (Fig. 1, *A*). Because we were not certain of the diagnosis, the procedure was repeated one week later (Fig. 1, *B*). At this time an increase in the A-V block had occurred, and, during these intervals, definite flutter waves could be seen. There was otherwise no change in the second electrocardiogram. Unfortunately, we were unable to trace this patient and nothing is known of his clinical course.

CASE 2.—L. M. This patient was a 67-year-old man. He had suffered from syphilis for many years and a diagnosis of syphilitic aortitis had been made. Prior to 1935 numerous electrocardiograms had been perfectly normal. Fig. 2, *A* shows

the electrocardiogram during an attack of tachycardia in 1935, and Fig. 2, *B*, a similar attack in 1936. Shortly thereafter the patient died suddenly in his home, and no post-mortem examination was done. We believe that both of these tracings show auricular flutter with interventricular block (left bundle branch block type). There is also a variable degree of A-V block. In Fig. 2, *A* it is rather regular, and alternates between a ratio of 2:1 and 3:1.

CASE 3.—R. L. K. This 67-year-old man was seen shortly after the onset of an attack of tachycardia which followed acute posterior myocardial infarction. Fig. 3 shows the electrocardiogram which was taken during this attack. Fig. 4 shows later

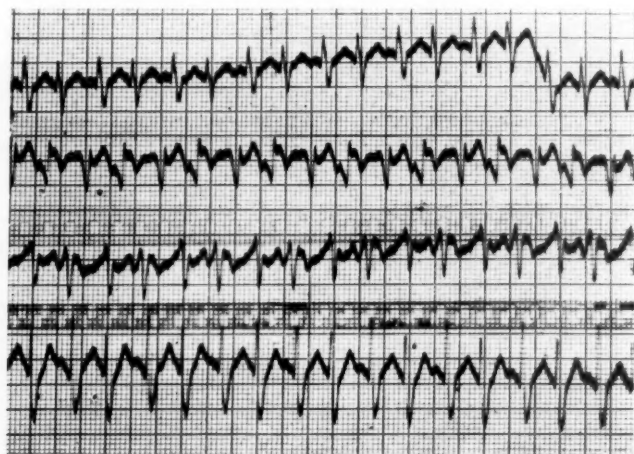
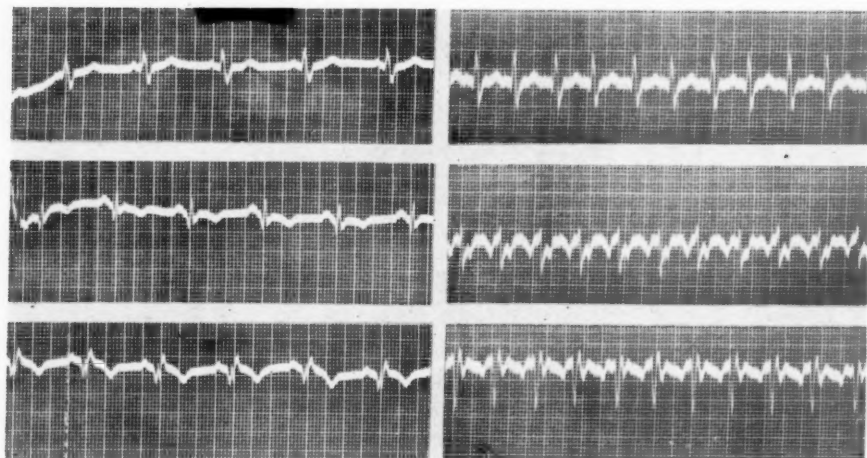


Fig. 3.



A.

B.

Fig. 4.

electrocardiograms on this patient during a period of normal rhythm and during another attack of tachycardia. In the latter case it is obvious that auricular flutter with 2:1 block is present, plus a deformity of the QRS complex. Going back to Fig. 3, one can see the similarity, and it becomes apparent that this is a record of

auricular flutter, with a deformity of the QRS and T waves caused by acute myocardial infarction. This patient has remained well, but continues to have attacks of paroxysmal auricular flutter. The form of the QRS and T remains unchanged.

CASE 4.—J. N. This 56-year-old man was admitted to Welfare Hospital because of chronic pulmonary fibrosis. An electrocardiogram shortly after admission showed (Fig. 5) auricular flutter with a wide QRS complex of the right bundle branch block type. It was only when the 2:1 block increased to 3:1 and 4:1 that the underlying flutter waves could be seen. Repeated electrocardiograms on this patient have shown several interesting changes. The first was a return to normal sinus rhythm, with the same QRS configuration. Then, for a time, the QRS complexes also became perfectly normal, and now the patient again has a right bundle branch block with sinus rhythm.

#### DISCUSSION

It is clear from the above illustrations that the diagnosis of auricular flutter in the presence of deformed QRS complexes is difficult only when the ventricular rate is rapid. Thus, it is probably a wise procedure in cases of tachycardia to apply carotid sinus pressure while the electro-

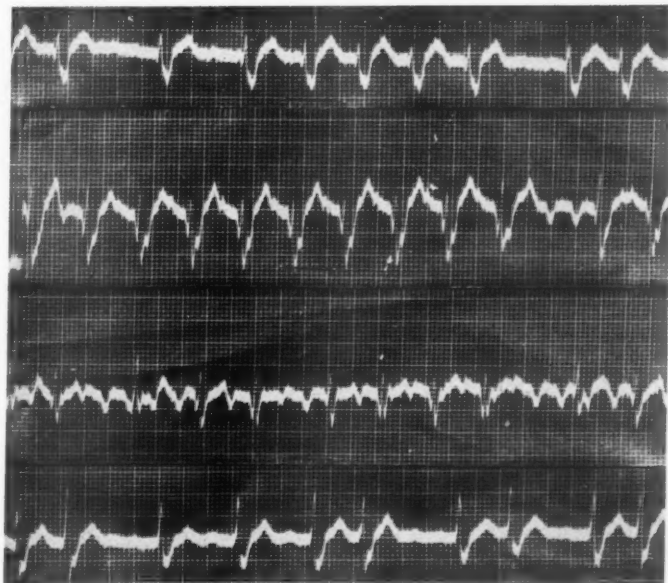


Fig. 5.

cardiogram is being recorded. In our experience, nodal tachycardia rarely, and ventricular tachycardia never, is affected by this form of vagal stimulation. Auricular tachycardias will often terminate, and in auricular flutter the block may be increased sufficiently to reveal definite flutter waves.

Any widening of the QRS complex, with or without marked deformity of the T waves, seems to interfere with the interpretation. Also, the changes in the S-T segment after acute myocardial infarction may cause

difficulty, particularly with posterior lesions, when the changes predominate in Leads II and III, for it is also in these leads that the auricular flutter waves are usually best seen.

As a general rule, ventricular tachycardias show a very constant wave form, whereas tachycardias caused by auricular flutter, with deformity of the QRST complexes, often show variations in the QRST complexes from beat to beat because of interference by the flutter waves. We have also found esophageal leads from the auricular level very helpful in the interpretation of this type of tracing.

#### SUMMARY

We have called attention to the difficulty of diagnosing auricular flutter in the presence of wide or atypical QRST complexes. In such cases the flutter may be mistaken for ventricular tachycardia. For proper therapy this differentiation is important.

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## THE INFLUENCE OF POSTURE ON THE ELECTROCARDIOGRAM

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FOR a number of years we have been making a comprehensive investigation of the cardiovascular adaptations which accompany the change from the horizontal to the upright position.<sup>1</sup> In most of these experiments the shift in position has been accomplished passively by means of a tilting table; the subject was suspended in such a manner as to eliminate all weight-bearing on the extremities. By thus minimizing the influence of muscular movements in aiding venous return against gravity, the strain on the circulatory system is accentuated and the consequent variations are accelerated. It soon became apparent that the subjects fell into three groups: (a) those who showed an accelerated pulse rate, a rise in diastolic pressure, and little or no change in systolic pressure, and were able to maintain the upright position under these conditions for relatively long periods (twenty minutes or more) without discomfort; (b) those with a more marked tachycardia and rise in diastolic pressure, and often a fall in systolic pressure, who usually fainted within this interval of time; and (c) subjects who, in spite of marked tachycardia, sweating, pallor, and lightheadedness, did not actually faint during the experimental period. A close correlation was found to exist between the level of muscular tone and the ability to maintain the upright position without developing signs and symptoms of syncope.<sup>1d</sup>

That the electrocardiogram of the normal subject varies with posture is a long recognized fact. Depression of the T wave has claimed particular attention—a phenomenon for which various explanations have been proposed. Recent studies suggest that the alterations in the electrocardiogram in the upright position are caused chiefly by changes in the contact between the heart and neighboring tissues.<sup>2</sup> There is still the question of the role of anoxemia of the heart muscle as a possible factor.<sup>3</sup> Since the tendency to faint, as it occurred in our experiments, was due to cerebral ischemia occasioned by a diminished cardiac output consequent to decreased venous return, it appeared probable that an electrocardiographic study of our subjects might indicate whether or not there was also a concomitant cardiac anoxemia.

Ten healthy adults, students and staff members, whose ages ranged from twenty-one to forty years, served as subjects. Four of these were classified as

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"fainters" because they were unable to maintain the upright position for twenty minutes; four showed little or no embarrassment during this period; two were classed as intermediate. The group of fainters included a member of the football team, a former football player, and a former member of the college boxing squad. The usual procedure was to take a control set of tracings with the subject in the horizontal position after a rest of at least fifteen minutes. Each set comprised the three standard leads and Lead IV F. As soon as the control electrocardiograms were completed, the subject was tilted, feet down, to the upright position ( $75^\circ$ ), and a second group of records was obtained. Four additional sets of tracings usually followed at five-minute intervals; the subject was returned to the horizontal position at the end of about twenty-three minutes. When syncope seemed imminent during this period, tracings were made before the blood pressure fell appreciably. Electrocardiograms were taken as soon as possible after the return to the horizontal position, as well as five and ten minutes later. Except in one instance, each subject was studied on at least two separate occasions.

All records were measured as suggested by Ashman and Hull.<sup>4</sup> The areas of the tracings were measured planimetrically after the records were projected to a magnification of approximately four times the original size.

#### RESULTS

*P wave.*—The changes in  $P_1$  were difficult to evaluate quantitatively because of the normally low voltage of the P wave in this lead, but there appeared to be a trend towards a slight decrease in height, beginning with the assumption of the upright position and continuing until the horizontal position was resumed. The changes in  $P_2$  were much more definite; the voltage usually increased immediately after the subject was tilted. In some experiments the voltage continued to rise, and reached, at the end of about ten minutes, a maximum value which was approximately double that of the control. In other instances, the maximum was not attained until the end of the F. D. (feet down) period. In five experiments, the initial rise was followed by a return to the control level after five or ten minutes; there was no further change during the F. D. period in three cases; in the remainder a secondary rise took place toward the end of the period. The resumption of the horizontal position was succeeded in most instances by a quick return to control voltage values. In one experiment, when the subject was tilted back to the horizontal, there occurred an immediate rise in voltage similar to that observed when he was raised to the F. D. position.

The most striking changes were observed in Lead III, in which tilting produced a marked increase in height in seventeen of the nineteen experiments (Fig. 1). This increase was usually maintained throughout the F. D. period, and the voltage at the end was at least twice that before or after tilting. Two subjects of the athletic type, one a fainter and the other an intermediate, showed a diphasic  $P_3$  in the horizontal position which became more positive when the upright position was assumed. The diphasic character persisted in the two experiments on each subject; in the second case the wave became entirely positive and approached the upper limit of normal voltage (0.20 mv.). In two sub-

jects there occurred a slight retardation of the upstroke of the wave and an acceleration in the speed of the down stroke, producing a scythe-like curve which became more pronounced as the tilting period was prolonged, and disappeared on return to the normal position. In two other subjects who evinced notching of the ascending limb of  $P_3$  when they were in the horizontal position, the notches became more conspicuous during the F. D. period.

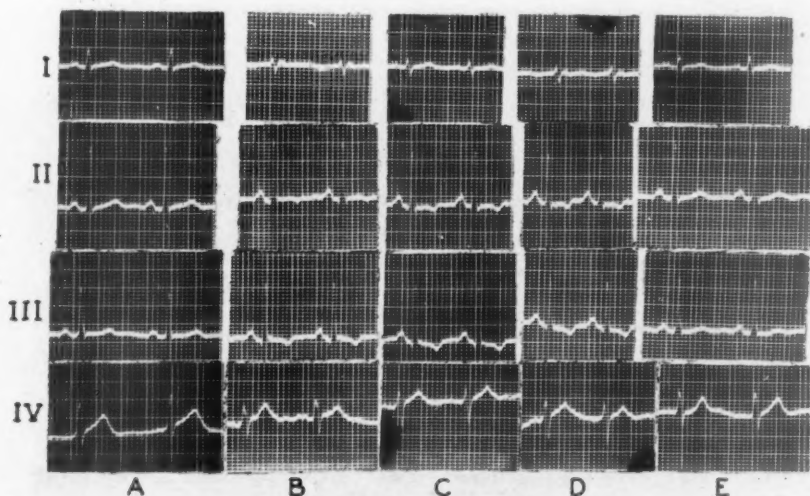


Fig. 1.—Subject J. A. G. Sthenic build. Intermediate. A. Control observations in the horizontal position; B. P. = 114/76; P. R. = 86; resp. = 22/min. B. Immediately after tilting; B. P. = 124/82; P. R. = 107; resp. = 22/min. C. Ten minutes after; B. P. = 118/82; P. R. = 111; resp. = 20/min. D. Twenty minutes after; B. P. = 122/84; P. R. = 132; resp. = 22/min. E. Control immediately after return to the horizontal position; B. P. = 112/78; P. R. = 94; resp. = 24/min. At C subject pale and sweating profusely; at D lightheaded.

*P-R interval and segment.*—Assumption of the F. D. position was accompanied in all but two cases by an immediate and progressive shortening of the P-R interval, amounting, at the end of ten minutes, to 10 to 20 per cent. This change was associated, but not correlated, with a variable and often decided increase in pulse rate. The lack of correlation was particularly evident in connection with the variations on the return to the horizontal position. At this time there was a bradycardia, particularly noticeable in the fainters (Fig. 3), but in only two cases was the P-R interval increased beyond control values.

Changes in the P-R segment were, for the most part, correlated with those in the P waves: a depression of the segment accompanied an increase in  $P_2$  or  $P_3$ . This depression, which may be interpreted as the auricular T wave, was also prominent in those cases in which diphasic P waves were present, and tended to become positive or isoelectric.

*QRS complex.*—Assumption of the F. D. position, in the majority of cases, resulted in an immediate decrease in the voltage of  $R_1$  and  $R_4$ ,

no consistent variation in  $R_2$ , and an immediate increase in  $R_3$  (Fig. 1). There was little further change during the F. D. position, except that  $R_1$  in the fainters was likely to show an additional, slight decrease. Three of these fainters gave evidence of an immediate, small decrease in  $R_3$ . Four athletic subjects (two fainters and two nonfainters) exhibited slurring or notching of the R waves in one or more leads. With the assumption of the F. D. position these slurs and notches, which often became more prominent, shifted in a counterclockwise direction (Fig. 2), and the shift, in several instances, increased progressively during the F. D. period.

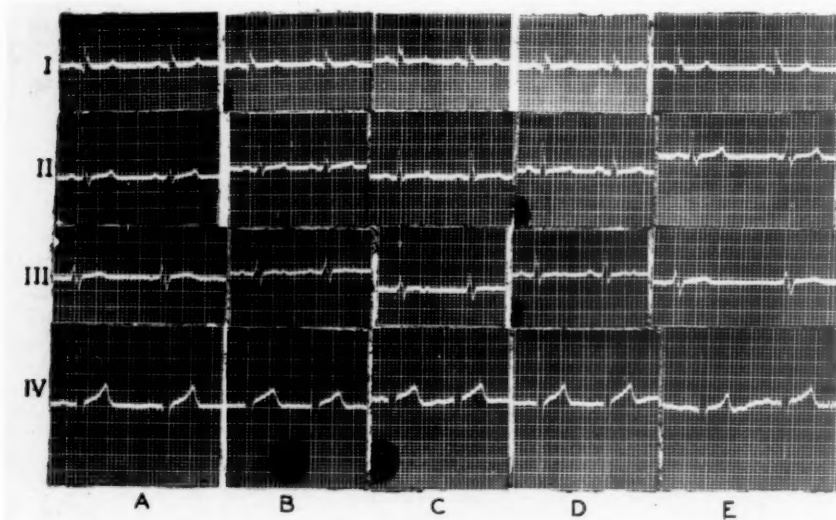


Fig. 2.—Subject T. G. Athletic build. Quarterback on football team. Fainter. A. Control observations in the horizontal position; B. P. = 116/72; P. R. = 72; resp. = 17/min., shallow and abdominal. C. Ten minutes after; B. P. = 118/78; P. R. = 95; resp. = 25/min., very deep. D. Twenty-three minutes after; B. P. = 103/88; P. R. = 100; resp. = 11/min., very deep. E. Control immediately after return to the horizontal position; B. P. = 122/88; P. R. = 69; resp. = 12/min. Subject dizzy at C; at D showed dry mouth, frequent swallowing, slight twitching; blood pressure sounds difficult to hear. Almost fainted as table was being tilted back to horizontal.

Tilting resulted in a decrease in the height of  $Q_1$  or an increase in  $S_1$ , whereas  $Q_3$  was generally increased and  $S_3$  decreased. With one exception, the fainting subjects revealed an increase in  $Q_2$ ; one subject also showed a rise in  $S_2$ . The changes in  $S_2$  were generally inconsistent;  $S_4$  was usually increased. The net area of QRS in Lead I diminished markedly when the upright position was assumed, and continued to diminish; the values in eight experiments were less than 40 per cent. of the control value after fifteen minutes of the F. D. period. No uniform differences were observed in the area in Lead II, although the duration of QRS inclined to diminish. The alterations in Lead III were likewise variable, but, in general, the areas characteristically increased on tilting; in several experiments they were over five times those of the control.

The area of QRS in Lead IV F definitely decreased. Calculation of the mean electrical axis of QRS from the areas in Lead I and Lead II showed deviation to the right in seven of the ten subjects (Fig. 4), no consistent variation in two subjects, and left axis deviation during the F. D. position in one of the fainters.

*T wave.*—With the exception of two experiments in which there was no change in Lead I, the records showed a striking decrease in the amplitude of the T wave in all leads.  $T_2$  was inverted in four experiments on two subjects (one fainter and one nonfainter), and  $T_3$  was inverted in all but three experiments. In many cases these changes were progressive during the F. D. position (Fig. 3); the T wave remained depressed when the subject was returned to the horizontal position, but increased to greater than normal value five minutes later. This was particularly true in the records obtained from the fainters.

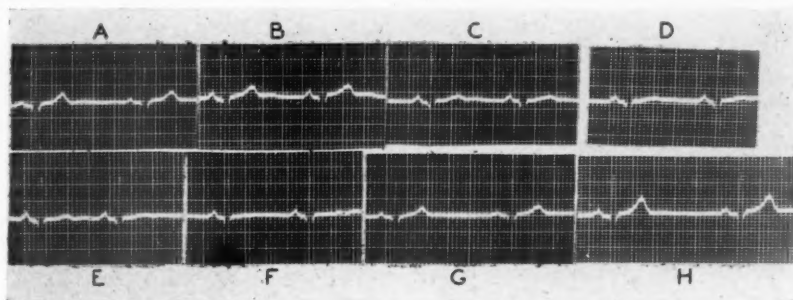


Fig 3.—Subject F. P. C. Sthenic build. Former member of boxing team. Fainter. Lead III. A. Control observations in the horizontal position; B. P. = 122/84; P. R. = 58; resp. = 10/min. B. Immediately after tilting; B. P. = 118/84; P. R. = 68; resp. = 10/min. C. Five minutes after tilting; B. P. = 122/90; P. R. = 72; resp. = 12/min. D. Ten minutes after; B. P. = 126/92; P. R. = 75; resp. = 14/min. E. Fifteen minutes after; B. P. = 120/94; P. R. = 79; resp. = 18/min. F. Twenty-four minutes after; B. P. = 120/110; P. R. = 83; resp. = 16/min. G. Two minutes after return to the horizontal; B. P. = 118/80; P. R. = 57; resp. = 8/min. H. Seven minutes after; B. P. = 120/72; P. R. = 60; resp. = 12/min. Mouth dry, light-headed, at C. At F fine tremors and twitching, particularly at shoulder, profuse sweating and imminent syncope.

In other instances the T waves were still lower than normal five minutes after the return of the subject to the horizontal position. These changes in the T wave were usually accompanied by a depression of the S-T junction which often amounted to more than 0.10 mv. in Leads II and III. There was also a propensity toward shortening of the duration of the S-T segment. With the exception of four experiments, there was a close correlation between the changes in the area and in the amplitude of the T wave. In these cases the appearance of the waves suggested that this was caused by an upward deviation of the S-T segment, which enclosed the same, or a slightly greater, area in spite of the flattening of the T wave. Calculation of the mean axes of the T wave indicated a definite left axis deviation which was much more pronounced than, and in the opposite direction to, the right axis deviation of QRS mentioned above. The difference in the direction of

the axes increased progressively, so that, at the end of the F. D. period, it was often well over  $100^\circ$  (maximum  $161.5^\circ$ ) (Fig. 4).

The area of the ventricular complex, QRST, tended consistently to diminish in Leads I, II, and IV F, and changed progressively during the F. D. period in some cases. Two nonfainters uniformly manifested an increase in the area in Lead III, but one gave no evidence of any significant change. The rest of the subjects evinced a definite decrease on being tilted, and a characteristic increase again at the end of ten to fifteen minutes of the F. D. period. Calculation of the mean axes (ventricular gradients) revealed deviations either to the right or to the left; the direction of the shift was roughly correlated with the changes in the QRS and T axes. In those cases in which the T axis changed slightly, the QRST axis was usually prone to shift to the right with the QRS axis; when the T axis varied appreciably in direction, the QRST axis veered to the left.

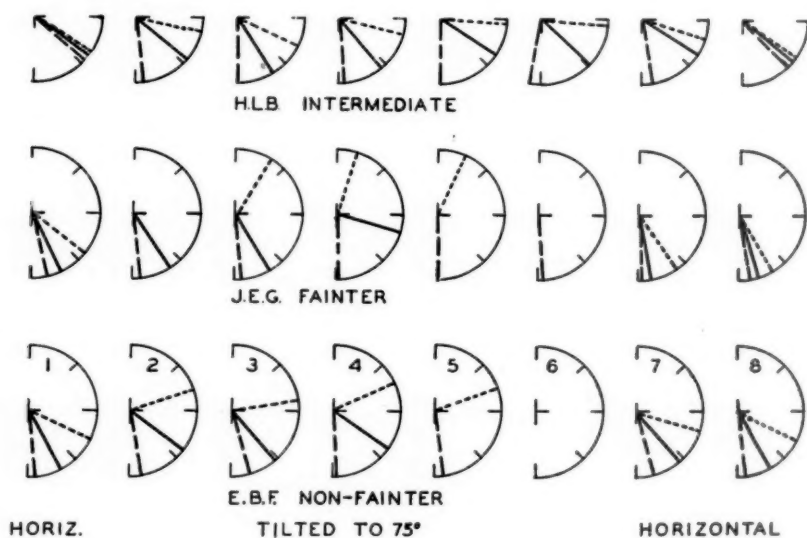


Fig. 4.—Changes in mean axes of ventricular deflections in the upright position. Solid line = average QRST axis (ventricular gradient); dashed line = average QRS axis; dotted line = average T axis. Control values are given in 1; 2 to 6 represent values, calculated from electrocardiograms, taken immediately, five, ten, fifteen, and twenty minutes, respectively, after tilting; 7 and 8 are values immediately and five minutes after return to the horizontal position.

#### DISCUSSION

The results described above suggest that there are two phases of response to the alteration in posture. When the subject is tilted to the upright position there is an immediate readjustment of the anatomic axis and a consequent reorientation of the electrical fields surrounding the heart. The right axis deviation which occurred in most of our experiments implies an anteroposterior rotation to the right, with a counterrotation to the left around the longitudinal axis.<sup>5</sup> This rotation

modifies the contacts with neighboring structures,<sup>6</sup> and may account, in part, for many of the changes, particularly those in the QRS complex immediately after, or soon after, the upright position is assumed. The subsequent variations during the maintenance of this position, however, cannot be explained in this way, for it is improbable that there are any further significant shifts in the position of the heart. These must reflect primarily the response of the cardiovascular system to the influence of gravity.

Among the factors in this response which might conceivably influence the electrocardiographic pattern are a decrease in venous return, changes in the rate and/or depth of respiration, and increased sympathetic activity. Alterations in heart volume do not seem to exert any significant influence, for the changes in the T wave persist after the return of the subject to the horizontal position, when the increased venous return unquestionably results in a larger heart volume. Although the alterations in the form of the T wave during the F. D. period bear a marked resemblance to those caused by the induction of anoxemia in normal hearts of the same age group,<sup>7</sup> the existence of actual anoxia of the heart muscle is questionable. Our failure to obtain more significant and consistent differences between the fainters and non-fainters, and the relatively quick return to the normal pattern after the subjects were returned to the horizontal position present arguments against this point of view. No correlation was found between respiratory and electrocardiographic changes. On the other hand, some degree of correlation was observed between the increase in sympathetic activity and the electrocardiographic changes. The assumption and maintenance of the F. D. position were usually accompanied by a fall in skin and subcutaneous temperatures, a rise in diastolic pressure, and a tachycardia which was often progressive.<sup>1b</sup> Fainters frequently showed marked pallor and profuse sweating. Nordenfelt<sup>8</sup> injected ergotamine into standing subjects and found that the usual postural changes in the electrocardiogram were thereby diminished or entirely eliminated, even though profound circulatory changes, leading to syncope, were taking place. Analysis of our data supports his conclusion that the strong sympathetic stimulation, which occurs as a compensatory response to the diminished venous return and the tendency to cerebral anemia (and anoxia), is a predominant factor in the production of the electrocardiographic deviations brought about by the upright posture.

The changes in the direction of the mean electrical axes indicate that, in addition to changes in conductivity, there are local variations in the excitatory process, and that these are determined by factors which are acting upon the same or different parts of the ventricular muscle with different intensities.<sup>9</sup> The nature of these factors is unknown, but they may possibly, in these experiments, be associated with the relative increase in sympathetic over parasympathetic activity.

The decrease in the QRST area and the change in the direction of the axes, associated with deviation of the QRS axis to the right, suggest the following explanation of the T-wave changes in terms of the conventional vector analysis.

The QRST area may be regarded as representing a sequence of repolarization which differs from that of depolarization, and/or an independent electrical effect. Theoretically, if the sequence of repolarization is the same as that of depolarization, and if the time course of repolarization is uniform, the net areas, above and below the base lines, of the QRS complex and the T waves must be identical, although opposite in direction, and the area of QRST in muscle of homogeneous properties should be zero. Therefore, a slight shift of the QRS axis to the right, accompanied by a marked decrease of the QRST area, should result in rotation of the T axis to the left, until, with a zero QRST area, the axis of the T wave is in the opposite direction and its area is equal to QRS. In other words, a reduction of the QRST area enables the "true" repolarization T wave to become a larger component of the total T wave and may account for the rotation of its axis to the left.

The correspondence between the theoretical expectation and our actual observations is striking. It suggests that, of the many factors which may influence the electrocardiographic pattern while the subject is in the upright position, the change in the position of the heart and the increased sympathetic activity may be primary.

#### SUMMARY

Series of electrocardiograms were taken on ten normal subjects before, during, and after passive tilting (feet down) to the upright ( $75^\circ$ ) position. The outstanding changes were an increase in the amplitude of the P wave in Leads II and III, a decrease in the amplitude of the T wave in all leads, a shift of the average QRS axis to the right and of the average T axis to the left, and a decrease in the QRST area.

It is suggested that the variations which occurred immediately after the assumption of the upright position were the result of a shift in the position of the heart and an alteration in its contacts with neighboring tissues. It is also suggested that, when further changes occurred during the maintenance of the upright position, they were due primarily to the increased sympathetic activity occasioned by the decreased venous return and consequent relative cerebral anoxia.

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## THE AURICULAR COMPLEX IN CORONARY THROMBOSIS

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THERE have been very few investigations of auricular complex changes in acute coronary artery disease. Master<sup>1</sup> observed enlargement of the P wave in his series of cases, and Pardee<sup>2</sup> implies that acute auricular dilatation may give rise to a large P wave. It is difficult to prove clinically that general cardiac dilatation occurs in acute coronary disease, and therefore it may be only theoretically assumed that local auricular dilatation takes place during the course of acute coronary occlusion. This study is based upon thirty-four cases of acute coronary occlusion which were observed at the Medical College of Virginia, Hospital Division, during the past seven years. In these cases the diagnosis was proved, both clinically and from the electrocardiograms. If an arrhythmia was present at the time of the initial tracing, the case was discarded. An auricular complex less than 0.2 millivolt in height and not more than 0.1 second in duration was considered normal.

In Table I a summary of the normal and abnormal complexes is given. No distinction is made as to the lead in which notching or enlargement of the auricular complex was present. It did occur more frequently in Lead II. In several cases the abnormality occurred in only one or two tracings. It was assumed that these departures from normal were actually due to the acute coronary occlusion, and that reversal to normal took place as the process improved.

In Table II an attempt is made to correlate the observations in these cases. Fifty-nine per cent of the patients had some deviation from normal in the P wave, 33 per cent had a transient or permanent notching of the P wave, and 26 per cent (nine cases) had unusually large, spiking P configurations. The duration of the P wave was within normal limits.

In the nine cases in which there were large auricular complexes, five, or 55 per cent, of the patients died. This was interesting in that the mortality in the cases in which the P waves were normal was only 29 per cent. Three of the patients with normal P waves died within the first twenty-four hours of hospital admission, and it is quite possible that they did not develop P-wave changes because of the short duration of the entire attack. The incidence of arrhythmias and conduction defects was much higher in those cases in which there was some P-wave abnormality, i.e., 27 per cent with notching, and 44 per cent with large P waves, as compared with 7 per cent with normal auricular complexes. Six patients died with arrhythmias or impaired conduction, and this was 75 per cent of the total number which developed arrhythmias.

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TABLE I  
CASES IN WHICH THERE WERE NORMAL P WAVES

CASE	LOCATION OF IN- FARCTION	DAY	P WAVE	COMMENT
1. Negro female Age 39	?	3 5 6	Normal Normal Normal	
2. White male Age 62	Anterior	1 2 7 21	Normal Normal Normal Normal	
3. White male Age 54	Anterior	1 2	Normal Normal	
4. White male Age 70	Anterior	1	Normal	Hospital death, one day after admission
5. White male Age 68	Anterior	12 hr. 1 5 6 10 17	Normal Normal Normal Normal Normal Normal	
6. White male Age 65	Posterior	1 2 4 15 25	Normal Normal Normal Normal Normal	
7. White male Age 42		2 3 5 41	Normal Normal Normal Normal	
8. Negro male Age 38	Posterior	1½ hr. 4 9	Normal Normal Normal	
9. White male Age ??	Posterior	1 hr. 1	Normal Normal	Hospital death
10. White male Age 55	Anterior	12 hr. 2 6	Normal Normal Normal	
11. White male Age 68	?	1	Normal	Hospital death, one day after admission
12. White female Age 67	Anterior	2	Normal	
13. Negro female Age 59		2 hr. 1 2 13 31 60	Normal Normal Normal Normal Normal Normal	
14. White male Age 68	Posterior	1 2 5 6	Normal Normal Impure auricular flutter Normal	Hospital death, 7th day
15. Negro male Age 37	Anterior	3 7 9 10 13 19 24 30	Normal Normal Notched Notched Normal Normal Normal Normal	Some signs of pericarditis

TABLE I—CONT'D

CASE	LOCATION OF INFARCTION	DAY	P WAVE	COMMENT
16. White male Age 53	Posterior	1 2	Notched Notched	Left hospital 2 days after admission
17. White male Age 51	Anterior	1 2 3 5 8 11 18 31	Notched Normal Normal Normal Normal Normal Normal Normal	
18. White male Age 50	Anterior	1 9 16 2 mo.	Normal Notched Normal Normal	
19. Negro male Age 45	Posterior	1 2 6	Auricular fibrillation Negative Notched	
20. White male Age 51	Posterior	6 hr. 1 4 9	Notched Normal Normal Normal	
21. White male Age 46	Posterior	5 7 13 23 6 mo.	Notched Normal Normal Normal Normal	
22. White male Age 67	Anterior	1 hr. 2 7	Notched Notched Nodal rhythm	QRS 0.12 sec., with nodal rhythm. Hospital death
23. White male Age 60	Anterior	2 17 30 4½ mo.	Normal Notched Notched Notched	
24. White male Age 68	?	4 hr. 7 21 50	Notched Negative Normal Normal	
25. White male Age 62	Posterior	1 4 8 11	Notched Notched Auricular flutter Auricular flutter	Hospital death
26. White male Age 58	Anterior	1 2 10	2.5 mm. 2.5 mm. 2.5 mm.	Complexes low. Returned to clinic 3 months after occlusion, wanting to go to work
27. White male Age 58	?	6 7 11 13 15 27	3.5 mm. 3.5 mm. Auricular flutter 3.5 mm. 3.5 mm. 3.5 mm.	Question as to quinidine intoxication. Arrhythmia stopped on discontinuing drug
28. White male Age 62	Anterior	4 5 6 7	3 mm. 2 mm. 2 mm. Normal	Bundle branch block. Partial A-V and bundle branch block. Hospital death 6/22/39
Occlusion 4 days on admission				

TABLE I—CONT'D

CASE	LOCATION OF IN- FARCTION	DAY	P WAVE	COMMENT
29. White male Age 48	Anterior	3	Normal	
		4	3 mm.	
		5	3 mm.	
		6	3 mm.	
		7	3 mm.	
		8	3 mm.	
		14	2.5 mm.	
30. White male Age 62	Anterior	12 hr.	2.5 mm.	
		2	2 mm.	
		3	Normal	
		4	2.5 mm.	
31. White male Age 68	Anterior	1	3 mm.	Partial A-V and bundle branch block. Hospital death
		2	10 sec.	
		3	2 mm.	
			Normal	
32. White male Age 71	?	1	Negative III	Partial A-V block. Hospital death
		3	Normal	
		5	3 mm.	
		7	Normal	
		11	Partial A-V block	
		14	3 mm.	
33. Negro male Age 41	Anterior	5	3 mm. high	Hospital death
		7	3.5 mm.	
34. White male	Posterior ?	2	2.2 mm.	Hospital death
		10	Normal	

TABLE II

I. Total cases	34	33% mortality	
Deaths	11		
II. Patients with normal auricular complexes	14	41	PER CENT
Patients with notching of P wave at variable intervals	11	33	
Patients with abnormally large P waves at variable intervals	9	26	
III. Deaths with normal P waves	4	29	
Deaths with notching P waves	2	18	
Deaths with large P waves	5	55	
IV. Normal P waves and development of arrhythmia or impaired conduction	1	7	(death)
Notched P waves and development of arrhythmia or impaired conduction	3	27	(2 deaths)
Large P waves and development of arrhythmia or impaired conduction	4	44	(3 deaths)
V. Deaths with arrhythmias or conduction defect	6	75	of total that developed arrhythmias

## DISCUSSION

In a small series of cases, departures from normal may have been chance occurrences. We are assuming in our thirty-four cases that the changes in the auricular complexes were significant prognostic factors. Master<sup>1</sup> and Pardee<sup>2</sup> agree that acute auricular dilatation may give rise to large auricular complexes, and one could assume that, if the acute coronary occlusion was of great enough severity, auricular damage would be more pronounced, and that therefore more deaths could be expected in the cases in which there was evidence of auricular change. The mortality was not increased in those cases in which there was notching or bifurcation of the P waves, although more of these patients developed arrhythmias. Bachmann<sup>3</sup> assumed that splitting of the P waves was due to impaired conduction through the interauricular bundle. He demonstrated a conduction bundle extending from the sinoauricular node to the base of the left auricular appendage. Pardee<sup>2</sup> states that notching of the P waves in one or more leads may be considered normal in about 25 per cent of healthy persons. Nevertheless, after the onset of acute coronary occlusion, it would seem that impairment of the conduction mechanism is added evidence of increased strain on cardiac function.

## CONCLUSION

Statistical percentages probably have very little value in a series of thirty-four cases, but we wish to present these two important points that we consider fundamental.

1. Any deviation from normal in the auricular complex, after acute coronary occlusion, is conducive to arrhythmias and impaired conduction.

2. The mortality rate in our series was almost doubled when a large, spiked auricular complex, over two millimeters in height, occurred during the course of the disease.

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## THE WELTMANN SEROCOAGULATION BAND IN MYOCARDIAL INFARCTION

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### INTRODUCTION

CLINICIANS and clinical pathologists are constantly searching for procedures which will aid in the diagnosis and prognosis of various diseases. Specific tests are the ideal, but many of these in the past have failed to fulfill the claims of their discoverers. Nonspecific reactions are frequently of value as diagnostic and prognostic measures. The serum coagulation test, first described in 1930 by Oskar Weltmann,<sup>1</sup> is an example of the latter. This reaction has to do with the effect of certain pathologic conditions on the coagulability of blood serum in the presence of electrolytes. It was applied by Weltmann<sup>2</sup> as a means of differentiating between obstructive and parenchymatous liver disease and between inflammatory and fibrotic processes. This serum coagulation phenomenon has since been studied by many European investigators,<sup>3</sup> and has found a place as a diagnostic and prognostic aid in their clinics. It attracted little attention in America until the past few years. Kraemer<sup>4</sup> reported his observations in diseases of the liver in 1935. Levinson, Klein, and Rosenblum<sup>5</sup> made a preliminary report of their study of approximately 1,200 children and adults with a variety of conditions. They called attention to the possibilities of this test and compared the Weltmann reaction with the sedimentation rate. The detailed reports made by them in 1938<sup>6</sup> and 1939<sup>7</sup> dealt particularly with the problem of differentiating between active and fibrotic pulmonary tuberculosis. Dees<sup>8, 9</sup> presented a clinical and experimental study of this reaction in 1940 and evaluated the fundamental factors involved in the phenomenon.

### THE TEST

Weltmann<sup>1</sup> observed that normal human serum, diluted to fifty times its volume with distilled water, did not coagulate when heated in a boiling water bath. When tap water was used, or when electrolytes, in the form of the chlorides of calcium, barium, or magnesium, were added to the serum, coagulation occurred upon heating. Inflammatory and exudative processes so altered the serum that coagulation occurred only in solutions containing high concentrations of the electrolytes. Chronic diseases characterized by fibrosis, the healing stages of acute infections, and parenchymal liver damage so changed the serum that coagulation also occurred in the more

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dilute solutions. On the basis of these preliminary observations Weltmann devised the serocoagulation test. In principle, the test is carried out by boiling in a water bath equal quantities of serum and graduated concentrations of bivalent electrolytes.

#### TECHNIQUE

The test is simple to execute, easy to control, and requires little apparatus and material. Simplified modifications and micromethods have been devised.<sup>9</sup> The following is the standard method described by Weltmann. Ten dilutions are prepared in 500 c.c. quantities from a stock solution of 10%  $\text{CaCl}_2 \cdot 6\text{H}_2\text{O}$ , namely, 0.1%, 0.09%, 0.08%, 0.07%, 0.06%, 0.05%, 0.04%, 0.03%, 0.02%, and 0.01%. These dilutions are numbered from 1 to 10, beginning with the most concentrated. Ten small (Wassermann) tubes are placed in a wire rack and also numbered 1 to 10. Into each are pipetted 5 c.c. of the corresponding dilution, and exactly 0.1 c.c. of unhemolyzed serum is added. The tubes are shaken to insure mixing of the contents and placed in a boiling water bath. In fifteen minutes the tubes are removed and examined. The highest dilution producing coagulation is observed. Flocculation, rather than turbidity or opalescence, is read as the end point. The number of tubes in which coagulation occurs determines the coagulation band (C.B.) of that particular serum.

The coagulation band of normal serum regularly extends from the first to the sixth tube. Occasionally, partial flocculation is present in the seventh tube, in which case the coagulation band is  $6\frac{1}{2}$ . In infectious, exudative, or necrotic processes the coagulation band is shortened or may be entirely absent. This was designated by Weltmann as a "shift to the left." A lengthened band occurs in fibrotic processes and parenchymatous affections of the liver. This has been called a "shift to the right." When exudation and fibrosis occur simultaneously, the coagulation band is the resultant of the balance between the two processes. Thus, lobar pneumonia may produce a coagulation band of 1 or 2. In hepatic cirrhosis the coagulation band is frequently as high as 9 or 10. The coexistence of the two diseases might result in a normal coagulation band.

The fundamental physiologic and chemical factors involved in this coagulation phenomenon are obscure. Dees<sup>9</sup> pointed out that the literature furnished no definite clue to the physiochemical mechanism which determines the behavior of sera in different diseases. Weltmann<sup>1</sup> demonstrated that the albumin content of the solution is not the controlling factor, and that the ratios of the different serum proteins to each other have no relation to the length of the band. Fibrinogen appeared to play no significant role in the reaction because serum and plasma gave the same values. Klein, Levinson, and Rosenblum<sup>10</sup> found that the albumin-globulin ratio had little effect on the coagulation band. Alterations in the serum pH are reported to exert no demonstrable influence upon the coagulation band.<sup>7</sup> Dees<sup>9</sup> demonstrated that serum calcium levels are not the decisive factor in determining the length of the band, even though coagulation failed to occur when calcium was removed from the system *in vitro*. Calcium administered intravenously tended to prolong the coagulation band temporarily. Clinical condi-

tions characterized by alterations in blood calcium levels were accompanied by no change in the coagulation band.<sup>9</sup> Dees<sup>9</sup> suggested that serum lipids are a decisive factor in determining the length of the band. She drew attention to the short band in acute infectious states in which the blood fatty acids are low, and to the long band in anemia, leucemia, nephritis, and diabetes, in which there is an elevation of blood fatty acids.

#### MATERIAL AND METHOD

Our interest in the application of the Weltmann serocoagulation test to the problem of coronary artery occlusion was aroused by the parallelism between this test and the sedimentation rate and leucocyte count in other conditions characterized by tissue necrosis. Any procedure which could be relied upon to indicate the extent and severity of myocardial infarction would be of value. Several blood studies have already been applied in order to obtain information on this aspect of the problem. White<sup>11</sup> pointed out that the degree and duration of the leucocytosis are a useful indicator of the size of the myocardial infarct, and hence of prognostic value. Libman and Sacks<sup>12</sup> stated that leucocytosis is the most frequent significant feature of the condition. In only four of seventy-four cases reported by Levine<sup>13</sup> was there a leucocyte count of less than 10,000. Coffen and Rush<sup>14</sup> observed an elevation in the leucocyte count in all of their fourteen patients. Hamman<sup>15</sup> stated that the average leucocyte count in this condition is 12,000 to 15,000 and that rarely is the count more than 30,000. Levine<sup>13</sup> reported one patient who had a count of 34,500, and Hines<sup>16</sup> observed one case in which the total leucocyte count exceeded 10,000 for a period of twelve days. Goodrich and Smith<sup>17</sup> state that, in their entire series of coronary occlusion cases, 35,700 was the maximum leucocyte count. This patient died, and autopsy revealed a large myocardial infarct. Marked leucocytosis usually indicates extensive infarction, and therefore a serious prognosis. Rabinowitz, et al.,<sup>18</sup> observed an increase in the sedimentation rate which was most marked on the third to fifth days, and persisted longer than fever or leucocytosis. Goodrich and Smith<sup>17</sup> studied the filament-nonfilament count<sup>19, 20</sup> in patients with myocardial infarction and found that it gave information of distinct prognostic value which was superior to that obtained from the total leucocyte count alone.

In applying the Weltmann serocoagulation test in a preliminary way in several cases of myocardial infarction, we were struck by the shortening of the coagulation band. Frequently the "shift to the left" was so marked that flocculation occurred only in tube 1 or 2. It was then decided to follow several consecutive cases with frequent and simultaneous total leucocyte counts, filament-nonfilament counts, sedimentation rates, and Weltmann reactions. The blood specimens were usually

obtained between 9:00 and 11:00 A.M., and only from hospitalized patients. The results of these examinations were charted for each patient in order to compare all procedures. In graphing the Weltmann coagulation band, each square represents one tube of coagulation. The highest eosinophile percentage is recorded. This procedure was followed in twenty-four cases of coronary artery occlusion between September, 1939, and March, 1940. From this series we present twelve representative patients, of whom seven recovered and five died.

The Weltmann reaction has been studied in other cardiac conditions. The coagulation band is shortened in acute rheumatic fever<sup>9, 10</sup> and lengthened in cardiac decompensation.<sup>10, 21</sup> Several months after the completion of our observations, we found that Teuffl,<sup>21</sup> in Germany, had studied the same problem. He reviewed 27 cases in 1936 and added to these in 1937, but did not compare the various procedures which we employed. Our own work is entirely independent of Teuffl's observations. We have found no similar studies in the English, French, or American literature.

#### CASE REPORTS

CASE 1.—(Chart I) H. A., a white man, aged 76 years, with a past history of angina pectoris, was admitted to the hospital on the day of onset of severe substernal pain. The electrocardiogram indicated posterior myocardial infarction. The coagulation band was 8 on the second day, and fell to 4 on the eighth day. Non-filament counts and sedimentation rates were elevated, but returned to normal as the patient improved and healing occurred. Eosinophiles gradually rose from 1 per cent on the fifth day to 21 per cent on the twenty-third day.

Four and one-half months later he was readmitted, twelve hours after a recurrence of the substernal pain. He was cyanotic, in shock, and remained in extremis four days, when he died of myocardial insufficiency. Again the Weltmann coagulation band progressively fell from an initial 8. Fibrosis and myocardial insufficiency probably combined to prevent further shortening of the coagulation band during both attacks. Only 1 per cent eosinophiles appeared during this attack.

Autopsy showed many areas of myocardial fibrosis and softening, as well as a diffuse area of infarction in the posterior ventricular wall. Neither coronary artery thrombosis nor complete occlusion was demonstrated, although there were many points of marked narrowing as a result of atherosclerosis and calcification.

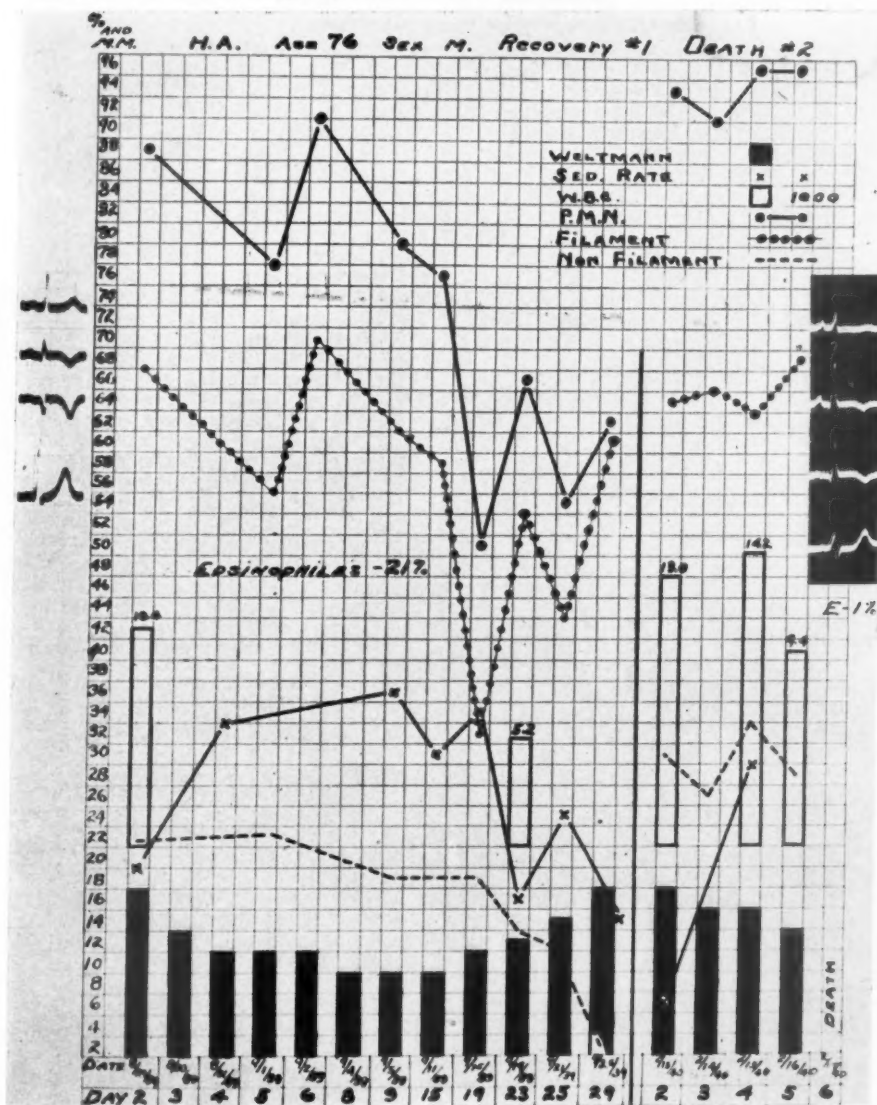
CASE 2.—(Chart II) D. B., a white man, aged 53 years, was admitted Oct. 20, 1939, five days after the onset of substernal pain. Clinical and electrocardiographic observations indicated myocardial infarction. Diabetes mellitus and acidosis were discovered and controlled. The falling coagulation band (from 6½ to 1½) and its persistent shortening, the increased nonfilament count, and the absence of eosinophiles indicated a poor prognosis. A decrease in the leucocytosis and in the sedimentation rate pointed to improvement. Repeated exacerbations of distress and shock occurred, and the patient suddenly died on the twenty-first day of his illness.

At autopsy the heart was enlarged, dark red in color, and covered by a shaggy, fibrinous exudate. A large area of recent infarction involved the posterior left ventricular wall from base to apex, and extended into the interventricular septum for one-half of its width.

CASE 3.—(Chart III) C. D., a white man, aged 46 years, was admitted to the hospital three days after the onset of epigastric and precordial pressure pain.

Clinical and electrocardiographic observations indicated myocardial infarction. The fall in the coagulation band from 4, on admission, to  $1\frac{1}{2}$ , the upward trend of the nonfilament count, and the elevated sedimentation rate pointed to a poor prognosis. Decreasing leucocytosis and this clinical course indicated improvement. He was found dead in bed on the twelfth day of his illness.

Necropsy revealed that the pericardium was filled with blood. In the anterior ventricular wall there was a large infarcted area which bulged forward with a hemispherical contour. Near the center of this aneurysm a large vertical tear was found. The descending branch of the left coronary artery was very atherosclerotic and almost completely occluded near the ostium.



CASE 4.—(Chart IV) R. J., a white man, aged 65 years, was admitted to the hospital nine hours after the onset of substernal pain. Clinical and electrocardiographic data indicated acute coronary artery occlusion. He grew steadily worse; myocardial insufficiency developed, and he died of general cardiovascular collapse on the third day of the illness. The shortening of the coagulation band from 6 to 4, the elevated sedimentation rates and nonfilament counts, and the absence of eosinophiles were all consistent with the outcome.

The autopsy, limited to the thorax, revealed a greatly hypertrophied heart. The coronary vessels were markedly sclerotic, and a fresh thrombus occluded the posterior

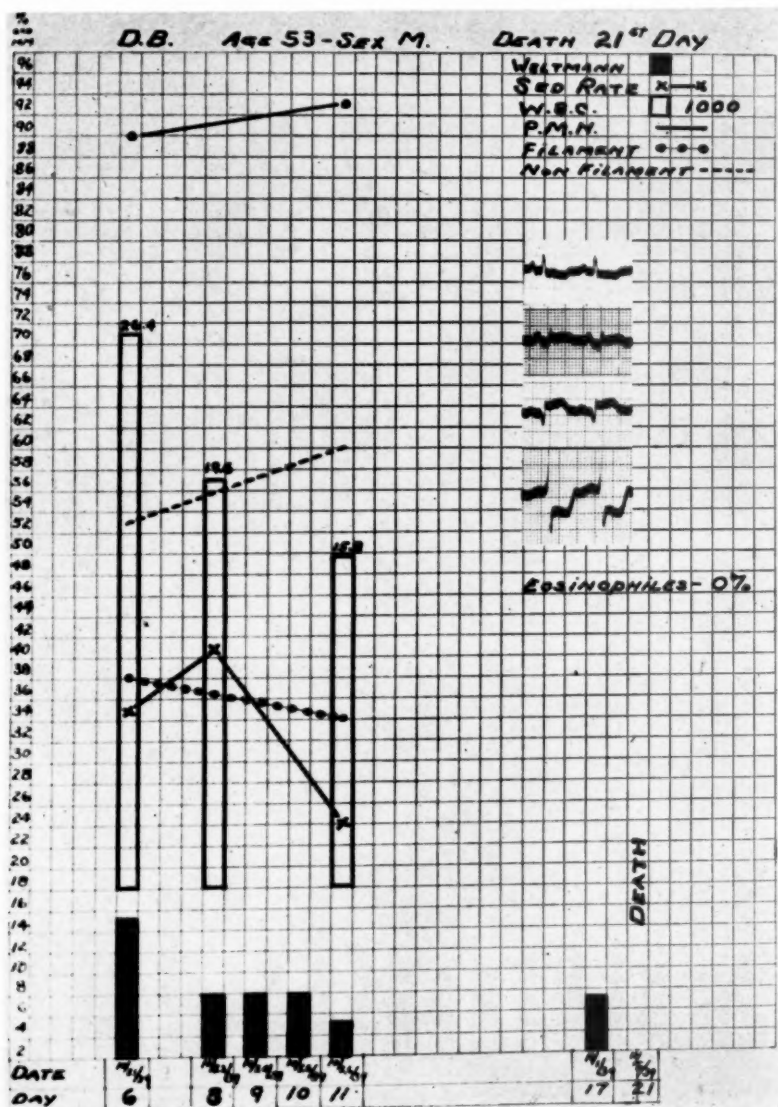


Chart II.—Pronounced "shift to the left," or shortening of the coagulation band in a case of severe infarction. Death on the twenty-first day. The sedimentation rate fell, indicating improvement.

coronary artery. There was infarction of a portion of the wall of the left ventricle at the apex. Beneath this was a mural thrombus in the tip of the left ventricular cavity.

CASE 5.—(Chart V) R. H., a white man, aged 48 years, was admitted to the hospital two hours after the sudden onset of severe epigastric pain, nausea, and vomiting. The differential diagnosis rested between acute coronary artery occlusion and perforating peptic ulcer. An electrocardiogram indicated myocardial infarction. The patient did not do well, developed myocardial insufficiency, and died on the thirteenth day of his illness after a recurrence of the chest pain.

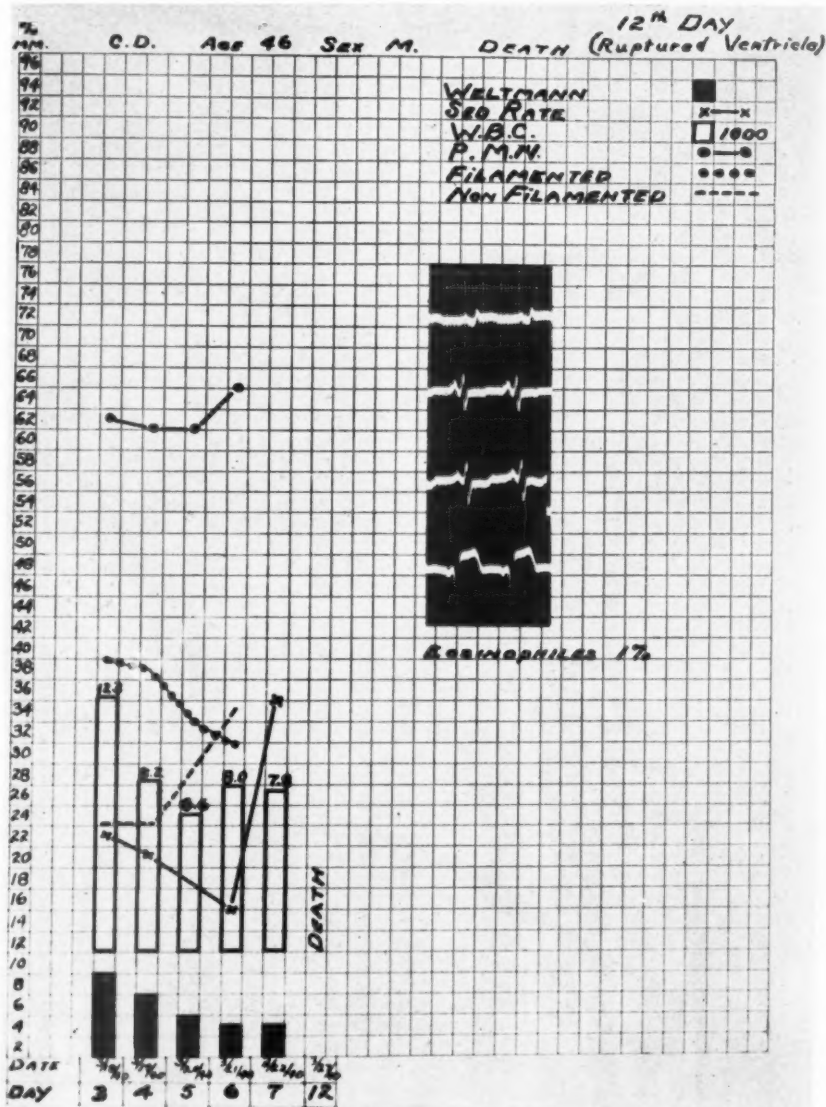


Chart III.—Another case of severe infarction, with a very short coagulation band; death resulted from ruptured ventricle.

In this case, the high leucocyte count, absence of eosinophiles, and rising sedimentation rate were more consistent with the clinical picture and outcome than were the nonfilament counts and the Weltmann reaction. Congestive heart failure undoubtedly prevented a more typical shortening of the coagulation band.

Autopsy disclosed infarction of the anterior wall of the left ventricle, the interventricular septum, and the posterior wall of the right ventricle. Each ventricular cavity contained a mural thrombus. The left coronary artery was markedly narrowed by atherosclerosis.

CASE 6.—(Chart VI) C. A., a white man, aged 54 years, who had had arterial hypertension for many years, first noted substernal pressure August 26, 1939, after

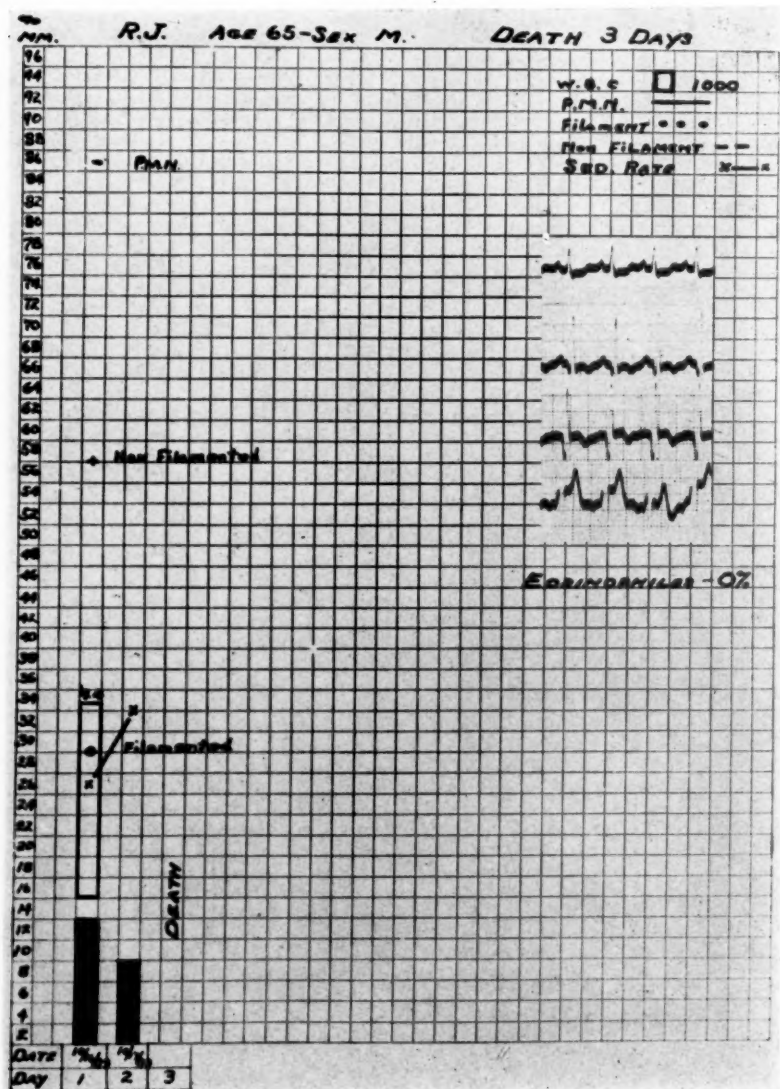


Chart IV.—Showing shortening of the coagulation band, high nonfilament count, rising sedimentation rate, and absence of eosinophiles.

a light breakfast. The distress radiated to both sides of the chest, and was relieved after five minutes by eructations, rest, and "Bisodol." During the next few days seven similar attacks occurred, all related to meals or exertion. On admission to the hospital, August 30, a diagnosis of angina pectoris or impending coronary artery occlusion was made. Since there were no significant changes in the electrocardiogram, Weltmann coagulation band, leucocyte count, nonfilament count, or sedimentation rate, it was felt that infarction had not occurred. Rest in the hospital resulted in a decrease in blood pressure and relief from the attacks. On September 2 he again experienced substernal pain which finally required morphine for relief. Electrocardiographic changes and shortening of the coagulation band,

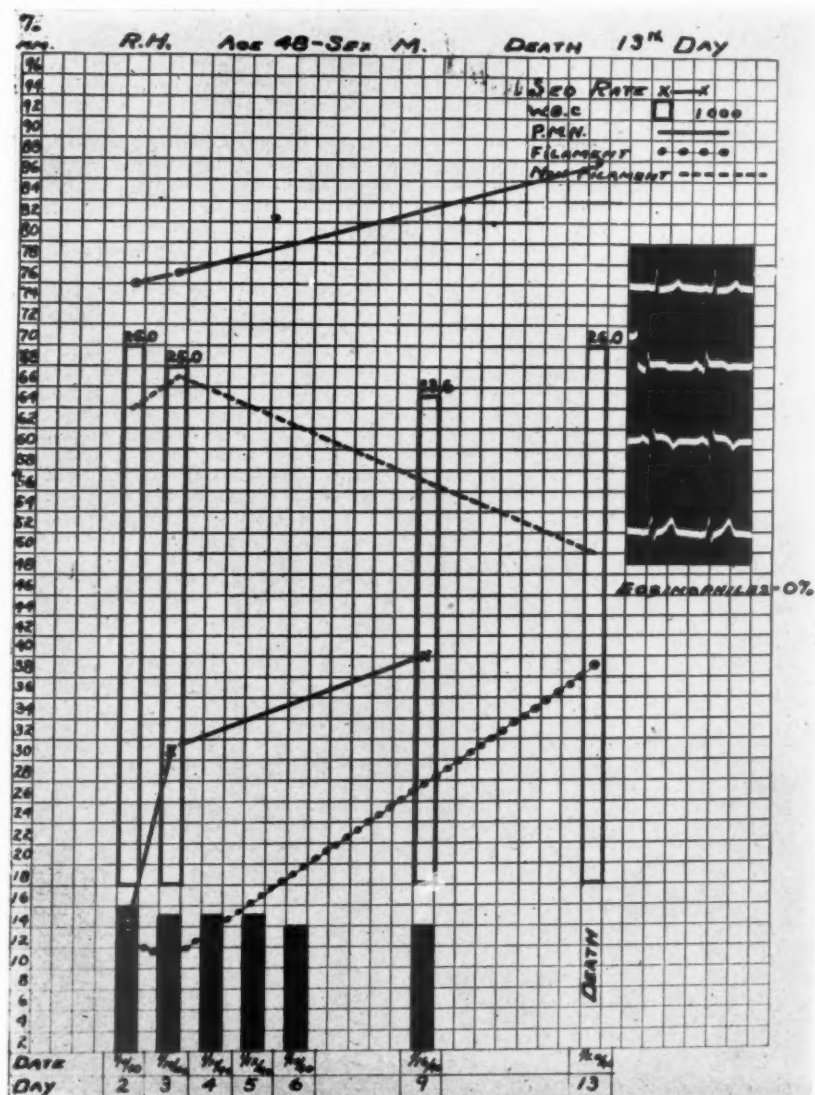


Chart V.—Showing only slight changes in the coagulation band, but high leucocyte count and rising sedimentation curve.

together with elevation of the leucocyte count, sedimentation rate, and nonfilament estimate, indicated myocardial infarction. His progress was satisfactory, and was accompanied by a gradual lengthening of the coagulation band and a decrease in the sedimentation rate and leucocyte and nonfilament counts. Eosinophiles appeared in the smear September 13, and reached 2 per cent.

CASE 7.—(Chart VII) T. K., a white man, aged 48 years, with a long history of gastrointestinal complaints and arterial hypertension, had had normal electrocardiograms since 1937. Symptoms of angina pectoris began in 1938. He was admitted to the hospital March 7, 1940, because of substernal distress which had

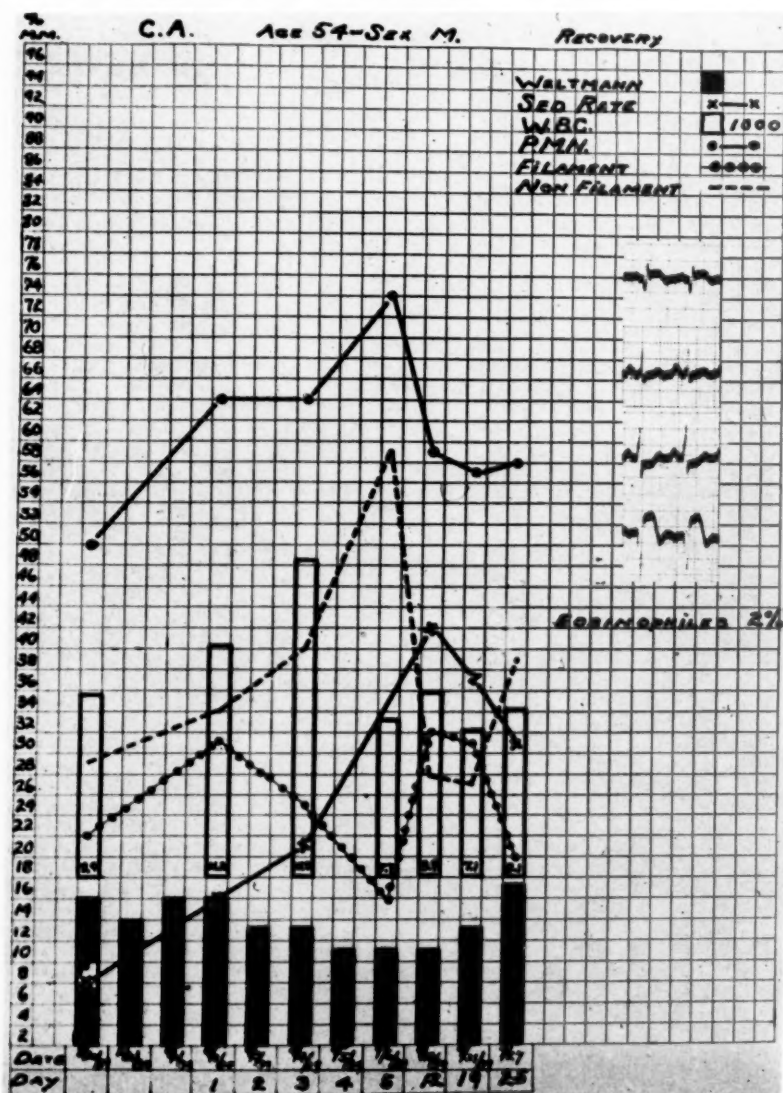


Chart VI.—Typical anterior infarction. Patient was admitted with severe coronary insufficiency, but did not show any changes in the electrocardiogram or coagulation band during first four hospital days. Infarction occurred on the fourth hospital day, and then typical changes, as shown, occurred.

been present since the previous evening, and had been partially relieved by nitroglycerine and codeine. Seven hours before admission the distress recurred, and morphine was required for relief. Electrocardiograms indicated myocardial infarction. The Weltmann coagulation band became shortened to  $4\frac{1}{2}$  on the third day and returned to normal by the thirteenth day. The sedimentation rate was elevated, but gradually fell. The eosinophiles reached 2 per cent. His hospital course was uneventful, and he was discharged on the twenty-fifth day of his illness.

CASE 8.—(Chart VIII) Seven days before admission this 48-year-old white man (G. S.) experienced gripping substernal pain which radiated through to the back and persisted for seven hours. He remained at home in bed, and was asymptomatic

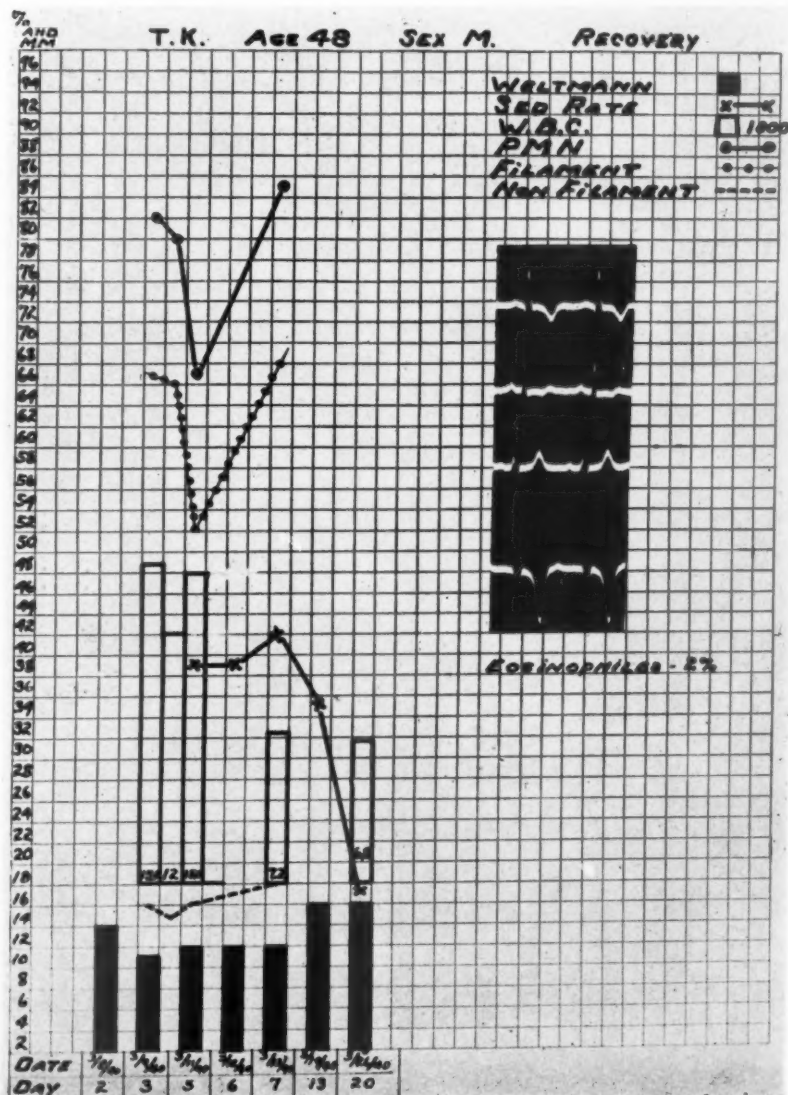


Chart VII.—Showing shortened coagulation band and high sedimentation rate and leucocyte count.

for two days. On the third day the pain recurred intermittently. On the day of admission the patient collapsed while en route to the bathroom. Electrocardiographic changes indicated anterior coronary artery occlusion. The Weltmann coagulation band became shortened to 4 on the sixth day, and then lengthened. The sedimentation rate and leucocyte count were elevated. Eosinophiles appeared on the tenth day and gradually rose to 9 per cent on the fourteenth day. His hospital course was uneventful except for a transient, presystolic gallop rhythm. The patient was discharged on the fifty-sixth day of his illness.

CASE 9.—(Chart IX) C. N., a white man, aged 48 years, was admitted to the hospital eighteen hours after the onset of a pressure sensation in the chest and

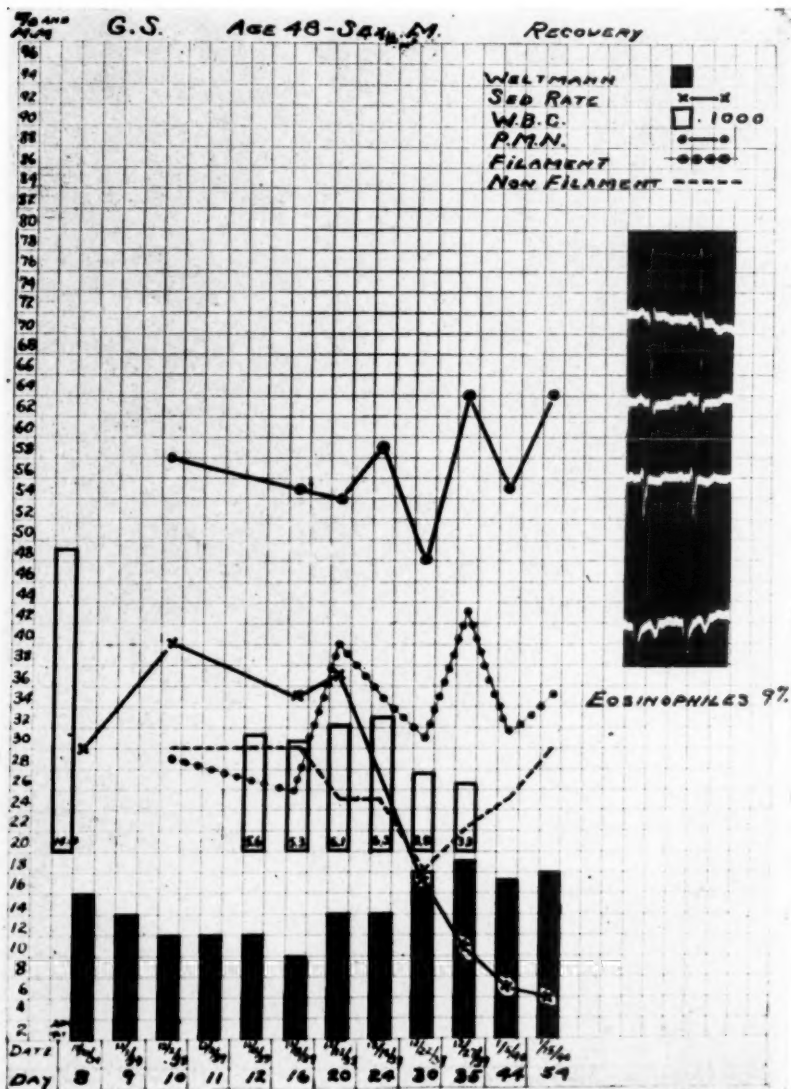


Chart VIII.—Showing typically high leucocyte count, elevated sedimentation rate, and shortened coagulation band. These returned to normal as healing occurred. Note high eosinophile count.

tightness in the throat. Twelve hours later these symptoms recurred. Serial electrocardiograms showed evidence of posterior coronary artery occlusion and transient auricular fibrillation. Weltmann coagulation bands of 4 and 2 were observed on the third and fifth days, respectively. Sedimentation rates, leucocyte counts, and nonfilament estimations were increased. All these slowly returned to normal. The lengthening of the coagulation band more closely paralleled the uneventful recovery of the patient. Eosinophiles appeared on the fifth day, but reached only 1 per cent. He was discharged on the twentieth day of his illness.

CASE 10.—(Chart X) Three days before admission to the hospital this 53-year-old white man (H. W.) experienced a severe, crushing pain in the left side of the

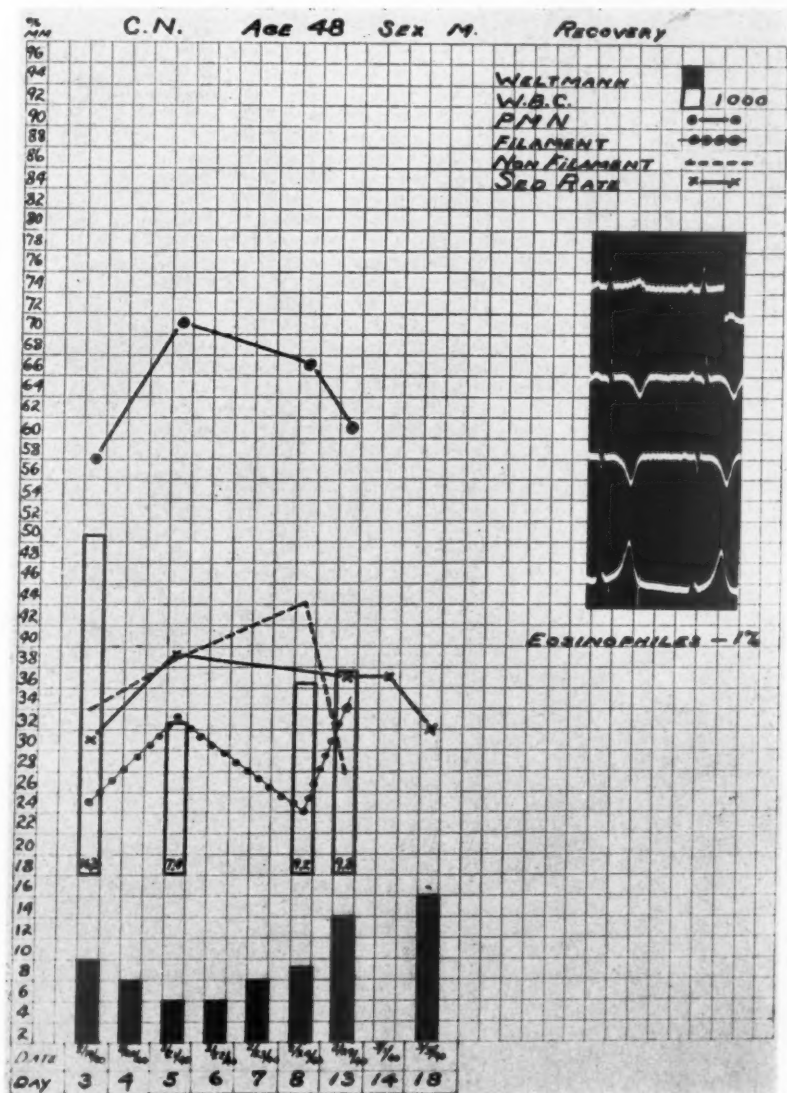


Chart IX.—Marked "shift to the left" in another case of severe myocardial infarction which returned to normal before sedimentation rate indicated healing.

chest which radiated to both arms. He had survived a coronary artery occlusion in 1933, and another in 1938. On admission he had acute cardiac asthma. Serial electrocardiograms indicated recent myocardial infarction. The falling coagulation band, elevated sedimentation rates, leucocytosis, and increased nonfilament counts paralleled a stormy course until the twelfth day of the disease. He then began to improve, had an otherwise uneventful convalescence, and was discharged on the sixty-second day of his illness.

The initial coagulation band of 7 and the succeeding moderate shortening in such a critically ill patient reflect the balance between the active myocardial necrosis and the fibrosis caused by the previous coronary artery occlusions. Healing of the recent infarction and the antecedent fibrosis explain the four final coagulation bands of 9.

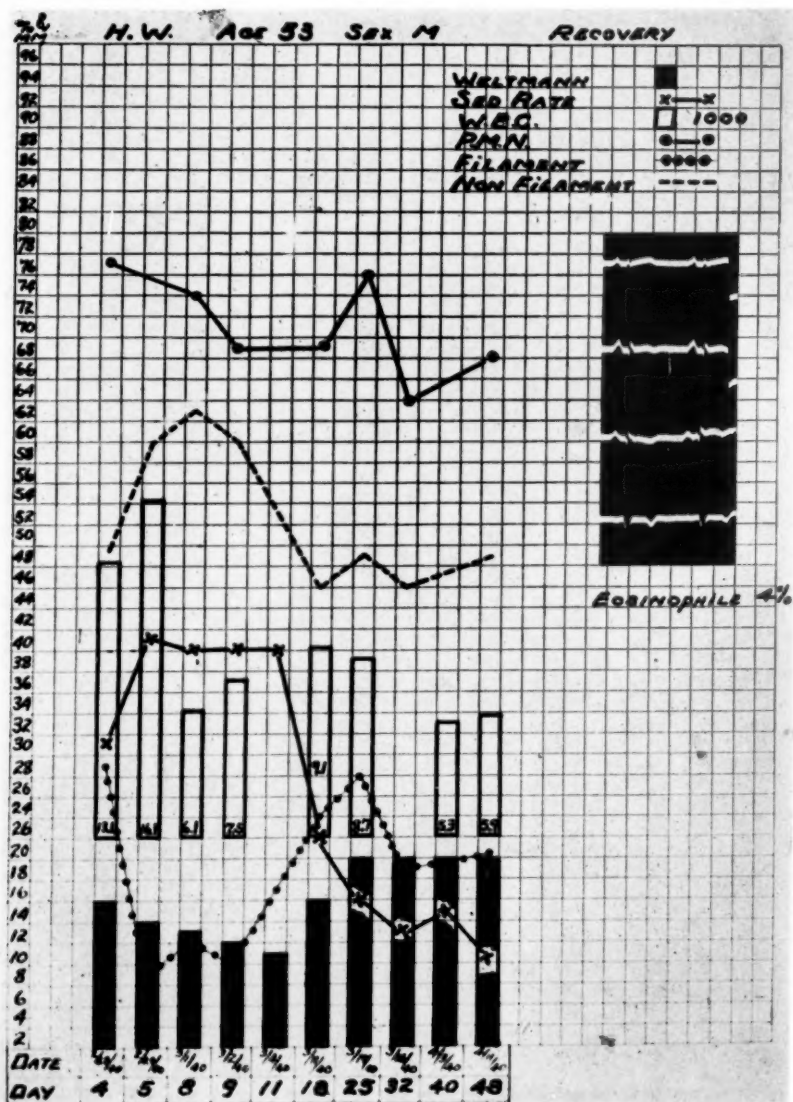


Chart X.—Showing progressive shortening of the coagulation band, high sedimentation rate, and a very high percentage of nonfilamented polymorphonuclears.

CASE 11.—(Chart XI) H. W., a white man, aged 50 years, was admitted to the hospital August 25, 1939, complaining of severe substernal pain of three hours' duration which required morphine for relief. Cholecystectomy had been done in April, 1939, because of chronic cholecystitis and cholelithiasis. Although he was in a critical condition, his recovery was uneventful except for the occurrence of ventricular extrasystoles which were controlled by quinidine sulphate. He was discharged on the thirtieth day of his illness. The coagulation band fell from an initial level of 8 to 3 on the fifth day, then gradually lengthened as the patient's condition improved.

CASE 12.—(Chart XII) Three weeks before admission to the hospital this 62-year-old white man (J. Mc.) began to have angina pectoris. Three days before

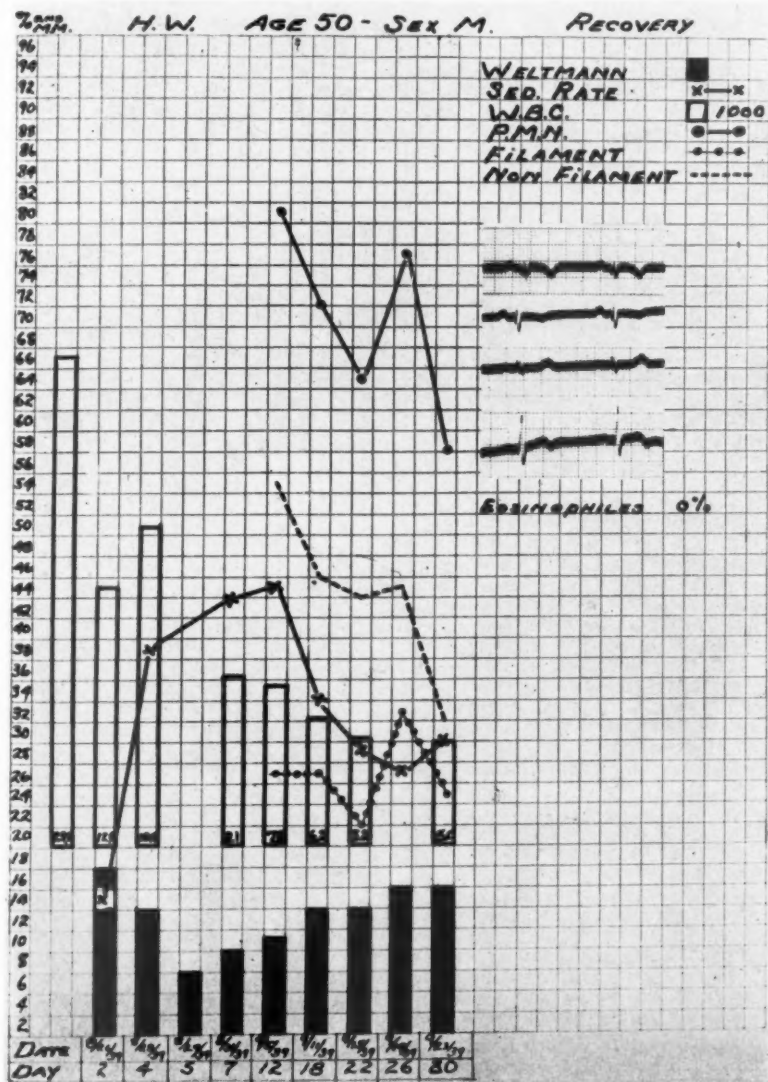


Chart XI.—Patient with extremely high leucocyte count and fairly marked shortening of the coagulation band, with return to normal after healing occurred.

admission the first of several prolonged attacks of substernal pain occurred; each lasted three to four hours. Clinical and electrocardiographic evidence indicated coronary artery occlusion. He was symptom free in the hospital until the seventh day of his illness, when he again experienced substernal pain, and his condition became grave. The electrocardiogram showed evidence of fresh infarction. On the twentieth day another, but milder, attack occurred. Thereafter his course was uneventful, and he was discharged on the forty-fourth day of his illness.

Note the rising Weltmann coagulation band and falling sedimentation rate on the fourth and seventh days. This would be expected with recovery from previous infarctions. The blood specimens were obtained before the infarction which oc-

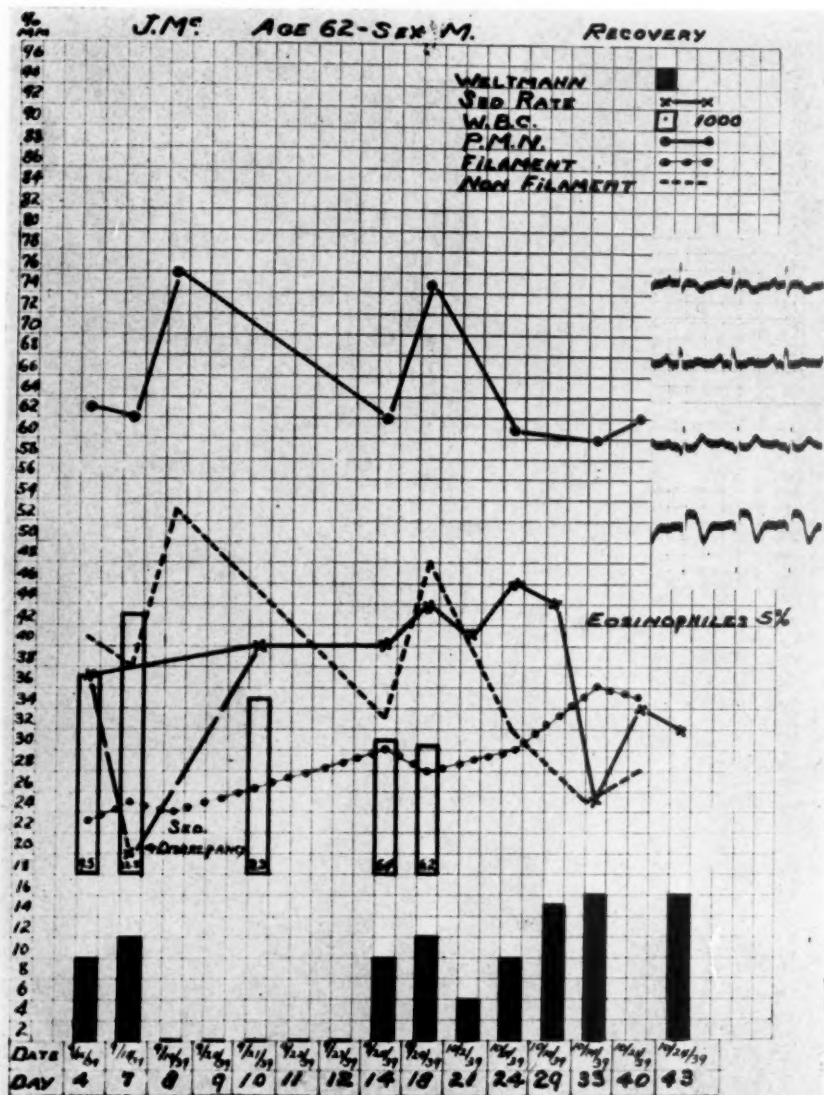


Chart XII.—Patient who showed complete absence of coagulation for ten days. Also note second occurrence of shortening after another infarction occurred on the twentieth day.

curred on the seventh day. After this attack, the coagulation bands remained markedly shortened while his condition was so critical. Here, too, the sedimentation rate, leucocyte count, and nonfilament estimates were increased. Eosinophiles appeared in the smear on Sept. 25, eight days after his first episode while in the hospital, and gradually rose to 5 per cent.

TABLE I  
SHOWING THE COAGULATION BANDS AS RUN PROGRESSIVELY IN TWENTY-FOUR CASES

CASE	COAGULATION BANDS												
1	8	6	5	5	5	4	4	4	5	5½	6½	8	
	8	7	7	6	(Death on second admission)								
2	6½	3	3	3	1½	2½	(Death)						
3	4	3	2	1½	2½								
4	6	4											
5	7	6½	6½	6½	5	5	(Death)						
6	7	6	7	7	6½	6½	4½	4½	4½	5½	8		
7	6	4½	5	5	5	4	6	6	8	8½	7½	8	
8	6	4½	5	5	5	7	7						
9	4	3	2	2	3	3½	6	7					
10	7	6	5½	5	4½	7	8	8	8	8			
11	8	6	3	4	4½	6	6	7	7				
12	4	5	0	0	0	0	0	4	5	2	4	7	8 8
13	8	6	2	2½	6	8	(Died 1 month later of second infarction)						
14	0	1½	2½	(Death)									
15	7½	7	6	7	7	8							
16	5	3½	4½										
17	5½	1½	0	2½	2								
18	6	5	5	5	5	5	5	5					
19	8	7	7	6	6	6	5½						
20	8	8	7	8	8	6							
21	8	8	7	7	4½								
22	8	7	7	6	6	6	7						
23	8	8	8	7	6	6	6	7					
24	7	6½	6	6	6								

Table I is a summary of the coagulation bands in the entire series of twenty-four cases. Twelve of these have been presented in detail. In the remaining cases the coagulation bands, clinical course, and outcome of the disease correspond to the observations in the twelve cases recorded.

#### DISCUSSION

The Weltmann serocoagulation reaction has been used as a nonspecific indicator of activity in a number of conditions. Many investigators have found empirically that the coagulation band is shortened ("shift to the left") in infections and other processes characterized by tissue destruction. When fibrosis has occurred the band of coagulation is lengthened ("shift to the right"). Since myocardial necrosis, followed by healing by fibrosis, is the sequence of events in coronary artery occlusion, it seemed likely that this nonspecific test would be a valuable aid in diagnosing and in following the progress of the condition.

In this study we have compared the leucocyte counts, nonfilament estimates, sedimentation rates, eosinophile counts, and Weltmann reactions in twenty-five cases of coronary artery occlusion. Twelve illustrative cases have been reported. During the early, acute stages of

the infarction, beginning on the second or the third day, the coagulation band became progressively shortened, and reached its minimum by the fifth to the seventh day. This "shift to the left" affords some index of the extent of myocardial necrosis. An abrupt, extreme (to tube 1 or 2), or persistent left shift would indicate either a large infarction or slow healing, and therefore a more serious prognosis. Conversely, a coagulation band which is only moderately shortened or promptly returns to normal has been found to be associated with satisfactory healing and a good prognosis. As repair proceeds by fibrosis, the coagulation band lengthens again to normal. Large areas of fibrosis, old or recent, result in a shift to the right, beyond normal, to tube 8 or 9 (as in Cases 8 and 10). The Weltmann reaction, then, is a manifestation of the actual pathologic course of the disease.

In the presence of coronary artery insufficiency which produces myocardial ischemia without actual infarction, the coagulation band is unchanged. The Weltmann test is useful in differentiating between these two conditions. This is well illustrated in Case 6. While still under observation in the hospital this patient had coronary artery occlusion, accompanied by a typical shift to the left.

We have compared the Weltmann reaction with the sedimentation rate throughout our series because the latter procedure has been so extensively used in following cases of coronary artery occlusion. The sedimentation rate is known to be increased by destructive changes in the body, as well as by repair, whereas the coagulation band is shortened by the former and lengthened by the latter. Certain physiologic conditions, such as normal pregnancy and the ingestion of food, alter the sedimentation rate. It may vary in the same patient at different times during the day. These variations are not observed with the Weltmann test, which more closely reflects the true nature of the pathologic changes and the clinical course of the patient.

Our observations on the eosinophile percentages in this group of patients are consistent with those of Goodrich and Smith.<sup>17</sup> In the cases of fatal occlusion they found no eosinophiles up to the fifth day. The number increased slowly to 1.6 per cent on the tenth day, and then fell to zero on the twelfth day. In the recovered group, eosinophiles appeared earlier and rose to 3.6 per cent on the fifteenth day.

The close parallelism between the changes in the Weltmann coagulation band and the nonfilament count is also to be noted. Our observations confirm those of Goodrich and Smith<sup>17</sup> that the average nonfilament count is higher in the cases of fatal occlusion than in patients who recover. The eosinophile and nonfilament counts are apparently related to the evolution of the myocardial infarction, and give valuable information in estimating the prognosis.

There are two complicating factors which must be considered in interpreting the coagulation band. The presence of fibrotic processes,

old or new, cardiac or extracardiac, may interfere with the "shift to the left" which is indicative of the true extent of the infarction. However, a careful past history and clinical study of each patient will clarify this point, as is illustrated in Cases 1 and 10. Myocardial insufficiency will also prevent as much shortening of the coagulation band as would otherwise be expected. This is illustrated in Cases 4 and 5. Careful examination of the patient should disclose this complication, and obviate any confusion in interpreting the Weltmann reaction under these circumstances.

We believe that the Weltmann serocoagulation reaction reflects the true evolution of myocardial infarction more accurately than any of the many other nonspecific tests now available. It is of distinct value in diagnosis and prognosis. By frequent charting of the coagulation band, together with the results of the other nonspecific laboratory tests, one obtains diagnostic and prognostic information which is superior to that gained from any one procedure alone.

#### SUMMARY

The serocoagulation test of Weltmann has been compared with other diagnostic and prognostic blood studies in coronary occlusion with myocardial infarction.

It compares favorably with these procedures.

With large infarctions a marked "shift to the left" in the coagulation band occurs, so that it is an index of degree of infarction.

Healing of the infarction can be followed by the progressive change in the coagulation band.

In certain conditions the sedimentation rate may be altered by other, coexisting causes. The Weltmann test is not altered in such a manner, and reflects either the healing phase or early exudative or destructive phase.

It can serve both as a diagnostic and prognostic laboratory aid to the clinician.

We wish to express our appreciation to Dr. F. Janney Smith, Physician-in-Charge, Cardio-Respiratory Division, Henry Ford Hospital, Detroit, Michigan, for his permission to study these cases and for his valuable aid in the preparation of this paper.

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## THE DIAGNOSTIC VALUE OF THE ELECTROCARDIOGRAM BASED ON AN ANALYSIS OF 149 AUTOPSY CASES

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**D**URING the course of the last two decades we have evolved a procedure of interpreting electrocardiograms which is based on our own experiences and those of others. We felt that the accuracy of our diagnosis of normality and abnormality in the electrocardiogram, as well as the specificity of the various patterns that we have come to recognize, should be subjected to critical analysis. Such an analysis can best be made, we believe, by comparing electrocardiographic diagnoses, judged independently, with post-mortem observations in a random series of autopsy cases. This should reveal the merits of the diagnostic criteria we have utilized, and thus demonstrate the accuracy and worth of these criteria. The following report deals with the results of such a study.

### MATERIAL AND PROCEDURES USED

All the autopsy cases in the files of the department of pathology from January, 1937, to May, 1940, were examined, and those in which electrocardiograms had been made were selected for this study. A total of 149 consecutive autopsy cases, with electrocardiograms, were obtained. In many of these cases serial electrocardiograms were available; some extended over a period of nine years.

After the autopsy cases had been selected, the electrocardiograms were analyzed independently as to their normality and abnormality, and the abnormalities were judged as nonspecific or specific with respect to the various patterns which we now recognize. In no case were the anatomic or clinical data consulted, and only the age of the patient was known; this was to insure an objective analysis according to our electrocardiographic standards. When serial electrocardiograms were available, the case was included only when the last tracing was taken shortly before the death of the patient. However, electrocardiograms which showed a cardiac strain pattern and were recorded within two months of the patient's death were not discarded. In 86 cases there was only one tracing; in 14 cases no chest leads were available; in 56 cases lead  $CF_2$  was the only chest lead; in the others both leads  $CF_2$  and  $CF_4$  were available. The limitations of single records and electrocardiograms without chest leads in differentiating patterns are obvious.

Once the electrocardiograms were classified, the interpretations were correlated with the anatomic reports, and it was decided whether or not the electrocardiogram and autopsy observations were in accord. In deciding whether cardiac hypertrophy was present, the patient's age, body weight, heart weight, and the thickness of the

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walls of the two ventricles were considered. Otherwise, the gross and histologic observations were used in making the correlation. The average normal heart weight was taken as 25 grams at three months, 125 grams at 12 years, and 200 grams at 17 years. In adults, weights of 300 and 250 grams, respectively, were considered the average normals for males and females. The average thickness of the ventricular wall was taken as 1.0 cm. for the left and 0.3 cm. for the right.<sup>1</sup> At times there was a discrepancy between the thickness of the ventricular wall and the heart weight. In such cases, more attention was placed on the weight of the heart than on individual measurements of thickness, for cardiac dilatation can decrease the latter. In borderline cases of heart weight, the decision was made by correlation with body weight.

The records were first divided into normal and abnormal electrocardiograms to see whether or not the anatomic changes were in accord; after this the various patterns we now recognize were catalogued separately and correlated as to discrepancy with the anatomic observations. All discrepancies were separated and analyzed in detail. The following patterns were separated from each other:

1. Normal record.
2. Nonspecific abnormal record.
3. Left ventricular preponderance without myocardial infarction.
4. Right ventricular preponderance without myocardial infarction.
5. Combined left and right ventricular strain without myocardial infarction.
6. Congenital heart disease.
7. Recent myocardial infarction.
8. Old, healed myocardial infarction.
9. Recent diffuse pericarditis without recent myocardial infarction.
10. Recent diffuse pericarditis with recent myocardial infarction.
11. Acute cor pulmonale.
12. Chronic cor pulmonale.
13. Mitral P wave.
14. Cor pulmonale P wave.

In our series there were no specific electrocardiographic patterns of acute diffuse glomerulonephritis, myxedema heart, hyperthyroid heart, beriberi heart, or chronic coronary insufficiency.<sup>2</sup> No separate classification of cases of prolonged electrical systole was made; this abnormality, like all others which did not fit into any of the specific patterns, was put under the heading of nonspecific abnormalities. The formula  $QRST = 0.39 \sqrt{C} \pm 0.04$  (where C equals cycle length) was used<sup>3</sup> to ascertain which electrical systoles fell within the normal range.

In several instances, records which showed more than one pattern were found as follows: Six were classed as right ventricular preponderance and mitral P wave, two were classed as recent myocardial infarction and recent diffuse pericarditis with recent myocardial infarction, two as chronic cor pulmonale and cor pulmonale P wave, one as mitral P wave and recent myocardial infarction, two as mitral P wave and nonspecific abnormalities, one as mitral P wave and left ventricular preponderance, one as mitral P wave and combined left and right ventricular strain, one as congenital heart disease and right ventricular preponderance, one as cor pulmonale P wave and combined left and right ventricular strain, and one as recent myocardial infarction and cor pulmonale P wave. Two were listed under three headings: One as combined left and right ventricular strain, chronic cor pulmonale, and cor pulmonale P wave; and the other as recent diffuse pericarditis without recent myocardial infarction, right ventricular preponderance, and mitral P wave. This made a total of 170 classifications for the 149 cases.

The final step was to classify the autopsy observations into separate categories and check the electrocardiographic patterns for each.

## THE CRITERIA USED FOR THE VARIOUS PATTERNS

Since the value of an analysis such as ours depends on the criteria used in classifying the records, it is worth while to describe them briefly. The details of most of these patterns are considered elsewhere.<sup>4\*</sup>

(a) *Records were regarded as normal* when the rhythm was of sinus origin without tachycardia (rate under 100) and without more than an occasional premature systole; when the P-R interval was between 0.12 and 0.21 second; when the QRS complex was 0.10 sec. or less in duration, did not show marked slurring or notching, and had an over-all dimension of more than 15 mm. (1.5 millivolts) in the limb leads; when the QRS pattern indicated absence of axis deviation or evidence only of right or left axis shift without evidence of ventricular preponderance (discussed below); when a Q wave (defined as an initial inverted phase of a diphasic QRS measuring  $\frac{1}{4}$  or more of the upright phase) was absent; when QRS was more than 8 mm. tall in leads  $CF_2$  and  $CF_4$ ; when QRS in lead  $CF_2$  had only two phases of the  $|/|$  type which were not less than 3 and 5 mm., respectively, in size; when QRS in lead  $CF_4$  had only two phases of the  $|/|$  type and the upright phase was not less than 3 mm., or when it had only one phase of the  $\wedge$  type, or when it had two phases of the  $|/|$  type or three phases of the W type with an initial inverted phase not more than 3 mm. in depth; when S-T depressions of not more than  $\frac{1}{2}$  mm. and S-T elevations of not more than 2 mm. were present in any of the limb leads; when S-T was isoelectric or elevated less than 2 mm. in leads  $CF_2$  and  $CF_4$ ; when T in Leads I and II was upright and not notched (provided it did not have the upright coronary T pattern); when T in leads  $CF_2$  and  $CF_4$  was upright and not taller than 8 and 10 mm., respectively. However, in analyzing the S-T and T deflections, the combined S-T-T complex was considered as a unit, and, when there was slight S-T deviation, the contour of the S-T-T was considered of more significance than the degree of the S-T deviation.

(b) *Records were regarded as showing nonspecific abnormalities* when they did not fit the foregoing description of normal and did not fall into any of the specific patterns. Certain arrhythmias, like heart block of various types, auricular fibrillation, frequent premature systoles, paroxysmal ventricular tachycardia, and nodal rhythm would also be placed in this group, even if the contour were normal. However, none of these arrhythmias occurred in this series in conjunction with a normal contour of the electrocardiogram.

(c) *Patterns of heart strain.* These were divided into three categories, namely, left ventricular preponderance, right ventricular preponderance, and combined left- and right-sided strain. Axis deviation attributable to the normal variant, axis shift, was excluded by the electrocardiographic appearance. Axis deviation associated with recent myocardial infarction or recent massive pulmonary embolism was also excluded because the axis deviation could have been attributed to the latter circumstances and not to cardiac hypertrophy. Similarly, axis deviation with a QRS duration of 0.12 sec. or more was not included, but was classed instead as a nonspecific abnormal curve showing intraventricular block.

The criteria for diagnosing *right ventricular preponderance* (lower part of Fig. 1) were a QRS duration of less than 0.12 sec.; absence of evidence of recent myocardial infarction or acute cor pulmonale; QRS in lead I mainly downward or equiphasic and of the S type (an S wave was defined as a second inverted phase of a diphasic QRS, measuring  $\frac{1}{4}$  or more of the preceding upright phase); QRS<sub>2</sub> upright, equiphasic, or mainly downward, with an S wave in the latter two circumstances; and QRS<sub>3</sub> mainly upright. This is distinguished from normal right axis shift, in which QRS<sub>1</sub> is mainly upright and small, or diphasic with an S wave less than the upright phase. The differentiation between the two patterns will become clearer by comparing right axis

\*Appropriate corrections were made for children.

†Inverted N.

shift (RAS) and right ventricular preponderance (RVP) in Fig. 1, in which typical patterns (including the S-T-T) are diagrammatically depicted.

The criteria for diagnosing *left ventricular preponderance* were those recently published from this department.<sup>5</sup> They fall into four categories, namely, type 1,

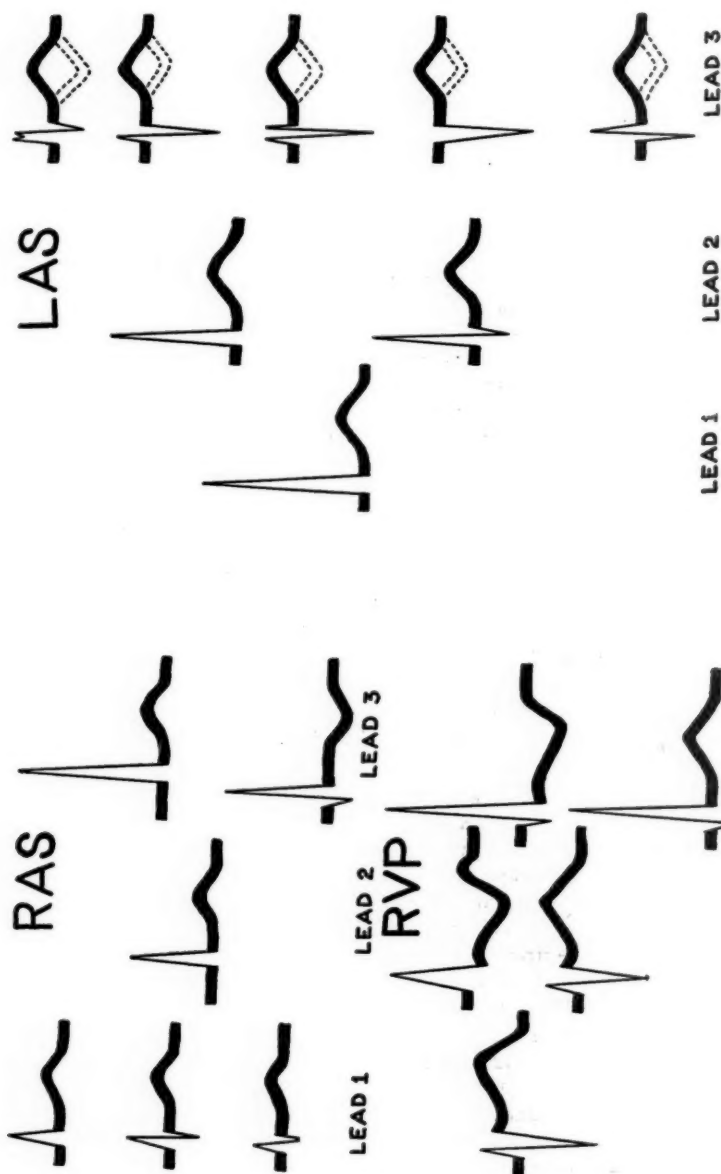


Fig. 1.—Diagrams of the typical appearance of the ventricular complex in the limb leads in right axis shift (RAS), upper part of figure, and in right ventricular preponderance (RVP), lower part of figure. In right ventricular preponderance, Leads II and III may also resemble the contours shown in right axis shift. Discussed in text.

type 2, mixed type, and concordant type. In all, QRS is less than 0.12 sec., and evidence of recent myocardial infarction and acute cor pulmonale is absent. In type 1 (Fig. 3) there is an upright, relatively tall  $QRS_1$ , associated with an inverted  $QRS_2$  or mainly inverted  $QRS_2$  of the S type, with a very small  $QRS_2$  (2 or

Fig. 2.—Diagrams of the typical appearance in left axis shift (LAS). The dotted lines in Lead III show alternative T wave appearance. All patterns shown would be normal except the lowest one in Lead III, which is usually abnormal. Discussed in text.

3 mm.) or a mainly inverted or equiphasic one of the S type, and without S-T-T abnormalities. In type 2 (Fig. 4) there are a tall, upright  $QRS_1$  and  $QRS_2$ , a depressed  $S-T_1$  (and  $S-T_2$ ), a low, diphasic or inverted  $T_1$  (and  $T_2$ ), and an inverted  $QRS_3$ . In the mixed type (Fig. 4) there is a combination of the QRS pattern of type 1 and

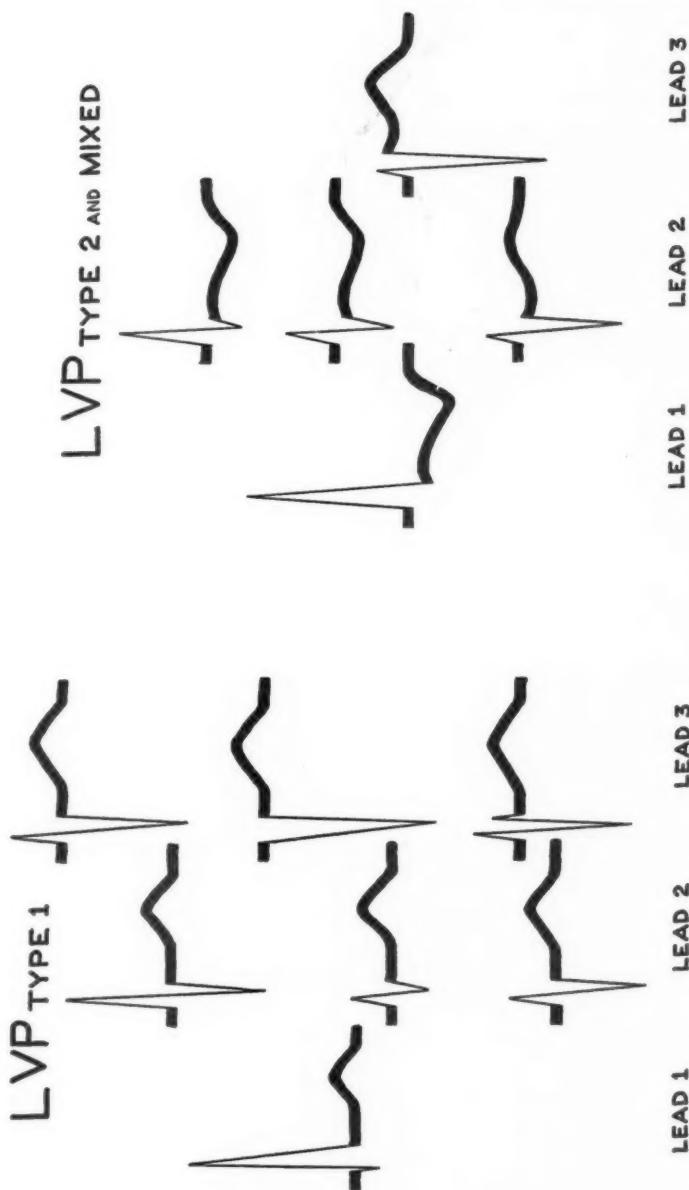


Fig. 3.—Diagrams of the typical appearance in the first type of left ventricular preponderance (LVP type 1). Discussed in text.

the S-T-T pattern of type 2. In the concordant type (Fig. 5), the S-T-T pattern is like that of type 2, but QRS is upright in all the limb leads. Left ventricular preponderance is distinguished from normal left axis shift, in which  $QRS_3$  is small, diphasic with an S wave, or inverted, but Leads I and II are normal in appearance.

Fig. 4.—Diagrams of the typical appearance in the second and mixed types of left ventricular preponderance (LVP type 2 and mixed). The upper curve of Lead II is encountered in the second type of left ventricular preponderance; the other two occur in the mixed type. Discussed in text.

The differentiation between left ventricular preponderance and left axis shift will become clearer by comparing Fig. 2 with Figs. 3, 4, and 5, in which typical patterns (including the S-T-T) are diagrammatically depicted.

The criteria for diagnosing *combined left and right ventricular strain*<sup>6</sup> were a QRS of less than 0.12 sec., absence of evidence of recent myocardial infarction and acute cor pulmonale, and the presence in the QRST complex of some features pointing to right, and others to left, ventricular preponderance. Two types of QRST would be placed in this group. In the first,  $QRS_1$  is small and diphasic,  $QRS_2$  is diphasic or mainly inverted, and  $QRS_3$  is inverted, with S waves in Leads II and III (and Lead I). A second type consists of a QRS pattern indicating right ventricular strain and an S-T-T pattern pointing to left ventricular strain.

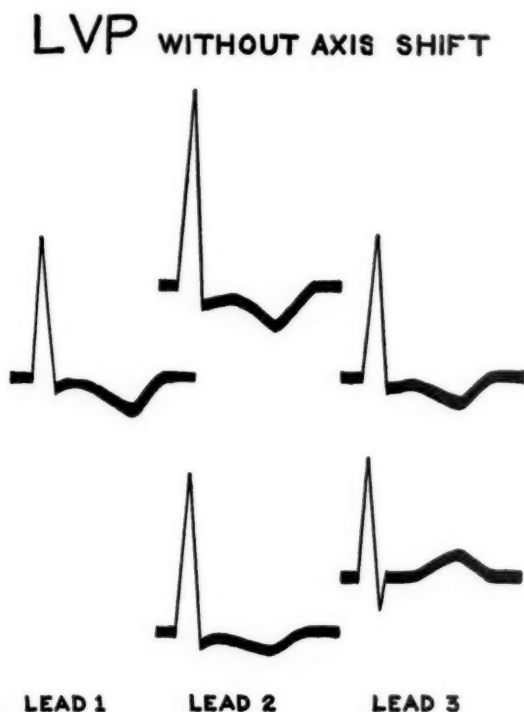


Fig. 5.—Diagrams of the typical appearance in the concordant type of left ventricular preponderance (LVP without axis shift). Discussed in text.

(d) *Congenital heart disease* was diagnosed when large, diphasic QRS complexes were present in two or all three of the limb leads.<sup>7</sup>

(e) The diagnosis of *recent myocardial infarction* was made when the generally recognized patterns of infarction were present in both limb and/or chest leads. The cases were listed as the anterior wall type, posterior wall type, combined anterior and posterior wall type, and atypical patterns. The details of diagnosis are discussed elsewhere at some length.<sup>4</sup>

(f) The diagnosis of *recent diffuse pericarditis with and without recent myocardial infarction* was made according to established criteria recently summarized elsewhere.<sup>8</sup>

(g) *Acute cor pulmonale* (massive pulmonary embolism) was diagnosed when the classical pattern of McGinn and White<sup>9</sup> was present, or when the classical picture described elsewhere in a report from this department<sup>10</sup> was found.

(h) *Chronic cor pulmonale* was diagnosed when, with right ventricular preponderance, *cor pulmonale* P waves (described below) were seen.

(i) The following two P-wave patterns were distinguished: The classical *mitral P wave*, indicative of chronic left auricular strain, in which P in Leads I and II were broad and notched and P<sub>3</sub> usually diphasic; and *cor pulmonale P wave*, presumably indicative of chronic right auricular strain, in which P<sub>2</sub> and P<sub>3</sub> were tall and peaked and P<sub>1</sub> was small.<sup>11</sup> These P-wave patterns were found to be associated with abnormalities of the QRS-T complex in this series.

#### DISCUSSION OF RESULTS

Attention should first be directed to the fact that this series is small; therefore, conclusions derived from it should be considered tentative pending similar analyses of much larger series. Nevertheless, even this small series permits several important deductions.

TABLE I  
THE RELATION OF THE ELECTROCARDIOGRAM TO THE AUTOPSY OBSERVATIONS

ELECTROCARDIOGRAPHIC PATTERNS	AUTOPSY OBSERVATIONS	
	NORMAL HEARTS	ABNORMAL HEARTS
8 Normal	7	1
141 Abnormal	0	141
149 Total	7	142

*The Accuracy of the Diagnosis of Normality and Abnormality.*—Table I shows the correlation of our autopsy and electrocardiographic interpretations in the 149 cases of this series. It will be seen that there were 141 abnormal electrocardiograms, and that, in all of these cases, there was evidence of cardiac damage at necropsy; this is a surprising degree of consistency, in that no electrocardiogram was abnormal when the heart was normal. This is a much better correlation than in a previous report,<sup>12</sup> and may indicate either (a) that this was a coincidence which would not occur if we had analyzed a much larger series, (b) that our criteria of abnormality of the heart at necropsy were not as rigid as those of previous workers, or (c) that our criteria of electrocardiographic abnormality were better than those of previous authors. It should be pointed out that the diagnosis of heart disease at necropsy was arrived at by us independently of the electrocardiographic interpretation. Only eight electrocardiograms were interpreted as normal, and in seven of these cases the heart at autopsy was also normal. In the eighth case, however, in which the electrocardiogram was regarded as probably normal (cf. Fig. 6A and Table III), the heart showed some coronary sclerosis with myocardial fibrosis and left ventricular hypertrophy; this person was 82 years of age.

The general deduction from these observations is that the electrocardiogram is a surprisingly good index of normality or abnormality of

the heart. But its value clinically is, of course, limited by the fact that it does not distinguish between clinical and subclinical forms of heart disease. Nevertheless, it is a surprisingly good index of the presence of anatomic damage in the heart.

*The Accuracy of Electrocardiographic Patterns in Revealing Specific Types of Heart Involvement.*—The 12 patterns which we were able to differentiate were correlated with the autopsy observations, and the degree of agreement is shown in Table II, together with the number of cases in which the diagnosis was not confirmed at necropsy. The details

TABLE II  
THE ACCURACY OF PATTERNS IN THE ELECTROCARDIOGRAM IN REVEALING SPECIFIC TYPES OF HEART INVOLVEMENT

ELECTROCARDIOGRAPHIC PATTERNS	NUMBER OF CASES	AUTOPSY OBSERVATIONS	
		AGREE	DISAGREE
Left Ventricular Preponderance Without Myocardial Infarction	33	30	3 1st showed old healed apical infarct, in addition to left ventricular preponderance. 2nd showed an organizing anterior infarct, in addition to left ventricular preponderance. 3rd showed recent septal and old healed apical infarcts.
Right Ventricular Preponderance Without Myocardial Infarction	12	12	0
Combined Right and Left Heart Strain Without Myocardial Infarction	3	2	1 It showed right ventricular hypertrophy only.
Congenital Heart Disease	3	3	0
Recent Myocardial Infarction	25	22	3 These 3 cases showed no infarct present.
Old Healed Myocardial Infarction	1	1	0 But disagreed as to localization.
Recent Diffuse Pericarditis Without Recent Myocardial Infarction	3	3	0
Recent Diffuse Pericarditis with Recent Myocardial Infarction	2	2	0
Acute Cor Pulmonale	1	1	0
Chronic Cor Pulmonale	3	3	0
Mitral P Wave	11	11	0
Cor Pulmonale P Wave	5	5	0

of the discrepant cases are assembled in Table III. The agreement between the electrocardiographic pattern and the necropsy abnormalities was surprisingly good; out of 102 instances in which there were specific patterns, the expected changes were found at necropsy in 94, and not found in 8. The number of specific patterns in this series was surprisingly large. In 81 of the 141 cases, one, two, or three specific patterns occurred, and, of these, there were one specific pattern in 58, two in 19,

and three in two. In the remaining 60 cases the abnormalities were non-specific.

Such agreement in so large a series of cases confirms the value of these patterns with respect to certain specific alterations in the heart, thus justifying continuation of the practice of distinguishing these patterns. In our experience, much of the error that creeps into the interpretation of electrocardiographic patterns is caused by the temptation to class a record in some specific pattern when it does not quite fit into that pattern. In our analysis we avoided this, so that the discrepancies which we found are real. Since the value of electrocardiography can be enhanced by an understanding of the causes of such discrepancies, the latter have been considered in detail (Table III, Figs. 6 and 7). The discussion can be facilitated by taking up each pattern in turn.

*Hypertrophy of the Ventricles.*—No attempt was made to diagnose ventricular preponderance in cases in which there was electrocardiographic evidence of recent myocardial infarction or acute cor pulmonale, or in the presence of intraventricular block. The pattern of the left, right, or combined ventricular strain was diagnosed 48 times. In all but one of these cases hypertrophy was present (cf. Table II). The one patient who did not have cardiac hypertrophy had a left ventricular preponderance pattern of the mixed type (cf. Case 3, Table III, and Fig. 6D). The preponderance pattern in this case could be attributed to the old apical infarct and its associated chronic coronary insufficiency, and the more recent septal infarction. Similarly, in two others with the second, or mixed, type of left ventricular preponderance, the electrocardiogram failed to reveal evidence of the old healed or organizing infarction which was found at necropsy (cf. Cases 1 and 2, Table III, and Fig. 6B and C).

In one of the three cases (Fig. 6E) in which the electrocardiogram was thought to show evidence of combined hypertrophy, only right-sided hypertrophy was found at necropsy. In this case the cause of the  $S_2$  and  $S_3$  contours is unknown. We have previously reported a case<sup>13</sup> in which the type I pattern of left ventricular preponderance occurred with brown atrophy of the heart. It would appear, therefore, that  $S_2$  and  $S_3$  may sometimes occur without left ventricular hypertrophy, and that, on occasion, the second, or mixed, type of left ventricular preponderance may occur atypically in coronary insufficiency in the absence of cardiac hypertrophy.

It is further interesting that, in the cases of cardiac hypertrophy, the electrocardiogram and necropsy observations were in accord as to the location of the dominant strain in the right and left side of the heart, with the one exception noted.

This is also shown in another way. In 44 of the cases of ventricular hypertrophy of which there were 51 at necropsy without myocardial infarction, acute cor pulmonale, or intraventricular block (Table IV),

there were evidences of one or another form of ventricular hypertrophy curve. In six others there was an axis shift, and in one there was none. These seven exceptions included a normal record, 5 nonspecific abnormal records, and 1 which showed only the pattern of recent diffuse pericarditis without recent myocardial infarction (which was confirmed at necropsy). Further, the agreement of the electrocardiogram in cases of isolated left or isolated right ventricular hypertrophy, as found at necropsy, was surprisingly good, namely, 21 out of 24 and 7 out of 8, respectively. It is, nevertheless, important to point out that hearts may be relatively large without producing any of the hypertrophy

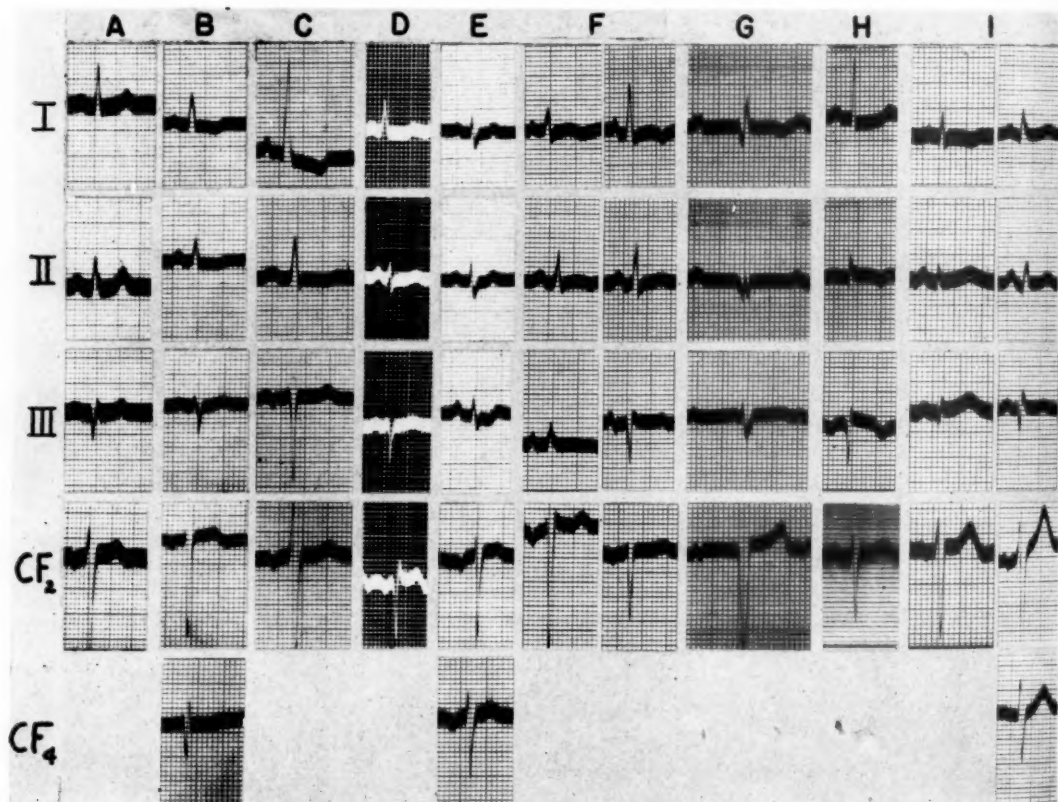


Fig. 6.—Portions of electrocardiograms in cases in which there were discrepancies between the electrocardiographic pattern and the anatomic changes. The details of each are summarized in Table III. Discussed in text. In *F* and *I*, two records from the case are shown; they were taken 3 days and 49 days apart, respectively.

patterns. Fig. 6Q is the record in a case in which the heart weighed 825 grams; there was hypertrophy of both ventricles but only left axis shift and nonspecific abnormalities in the electrocardiogram.

The results of this study indicate that cardiac hypertrophy may be revealed in the electrocardiogram by specific patterns. However, the patterns of left ventricular preponderance occasionally occur in the

absence of ventricular hypertrophy, and, contrariwise, ventricular hypertrophy occurs without the electrocardiographic patterns. Furthermore, on occasion, the dominant strain on the two ventricles is also not revealed by the electrocardiographic pattern, but in most instances the correlation is surprisingly good.

*Congenital Heart Disease.*—In all three cases of the classical type of congenital heart disease the diagnosis was confirmed at necropsy. However, 4 cases of congenital heart disease were found at necropsy in this series (Table IV); in the fourth case the electrocardiogram showed only right ventricular preponderance. The classical pattern, therefore,

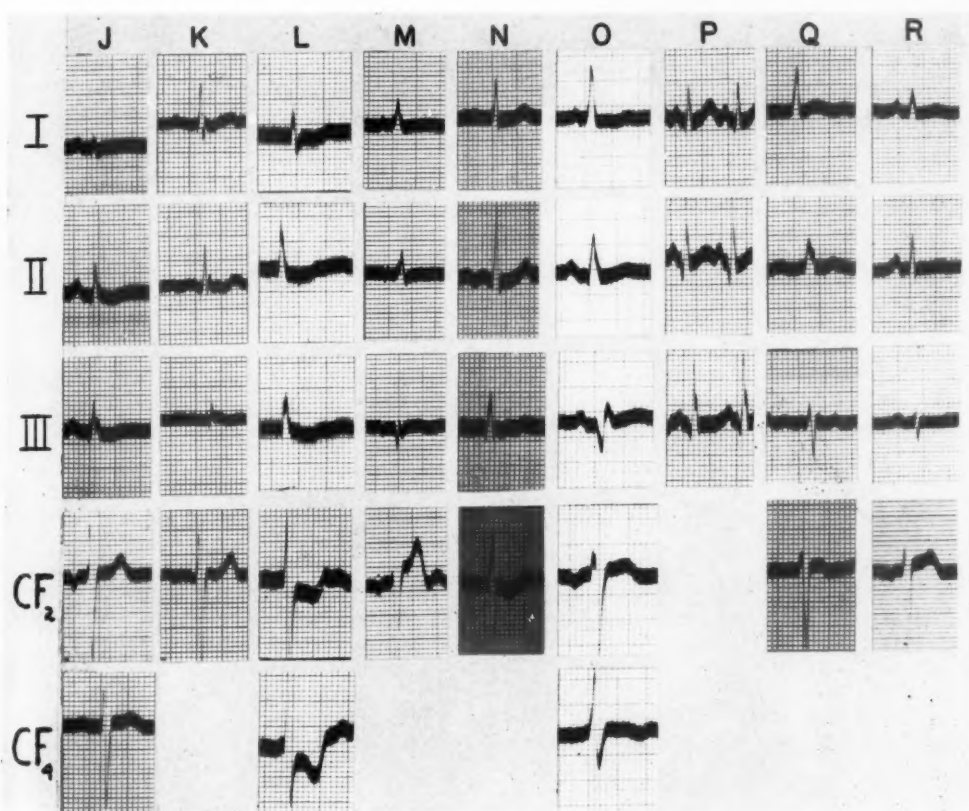


Fig. 6.

is diagnostic of congenital heart disease, but its absence does not rule out this condition. Schnitker<sup>14</sup> found this pattern in 30 per cent of 106 cases of congenital heart disease proved at necropsy.

*Myocardial Infarction.*—In twenty-five cases in this series there were various patterns of recent myocardial infarction, and in one case there was a stabilized coronary pattern indicative of an old, healed myocardial infarct. In 22 of the cases with the pattern of recent infarction

tion, the infarct was found at necropsy (Table II), and the age of the infarct agreed with the electrocardiographic evolution. In one, the case of old healed infarction, the infarct was found, but its location was inaccurately depicted (cf. Case 2 of anterior wall infarct type, Table III and Fig. 6*G*). In the other three cases, the electrocardiographic diagnosis of recent infarction was not substantiated at necropsy (Table III). In one case (cf. Case 1 of the anterior wall type, Table III and Fig. 6*F*), ventricular hypertrophy was found at necropsy and hypertension and terminal congestive heart failure were noted clinically; it would appear that terminal coronary insufficiency, accompanying the heart failure, gave rise to the coronary pattern and evolution.

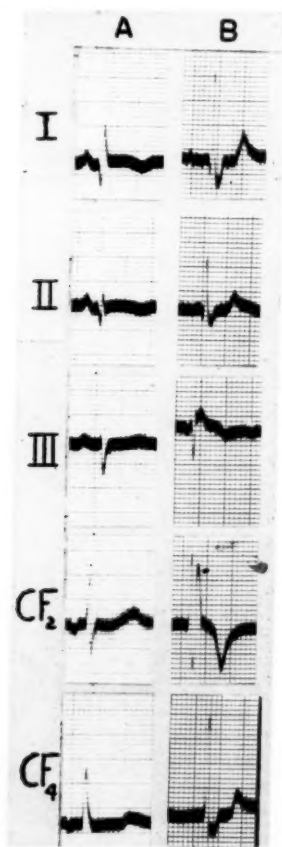


Fig. 7.—Portions of electrocardiograms in two cases in which the electrocardiographic pattern did not agree with the anatomic changes. *A* is a case of lateral wall infarction of the left ventricle in which the pattern described by Wood, Wolferth, and Bellet<sup>19</sup> did not occur. *B* is a case of massive pulmonary embolism in which there were nonspecific abnormalities in the form of intraventricular block of the second indeterminate (S) type. Discussed in text.

In the second case (cf. posterior wall type, Table III and Fig. 6*H*), the pattern was doubtless produced by the massive pulmonary embolism, superimposed on left ventricular preponderance, both of which were evident at necropsy. In the third case (cf. atypical pattern, Table

III and Fig. 6I), the suggestive pattern could have been caused by vitamin deficiency.

Thus there was surprising agreement as to the presence of infarction, its localization, and its age. This is in accord with a previous study.<sup>15</sup> The fact that an old, healed infarct was not correctly located may indicate that other circumstances had resulted in chronic coronary insufficiency in the region indicated by the electrocardiogram, but this is obviously a speculation. Further, it has been our experience that in some patients, especially patients with coronary disease, the electrocardiogram may imitate the coronary pattern during heart failure. We have also recognized the possibility that massive pulmonary embolism may give a coronary pattern, and other conditions, such as beriberi heart, may show atypical coronary patterns on occasion.

In this series, 25 cases of recent myocardial infarction were found at necropsy (Table IV); in 22 of these the diagnosis was made by means of the electrocardiogram, as stated above, and in three others it was not. Thus, not only may recent myocardial infarction be diagnosed in the electrocardiogram when it is not present, but also, on occasion, its existence is not revealed in the electrocardiogram. Of the 3 cases in which it was overlooked, there was only left ventricular preponderance in 2 (cf. Cases 1 and 3 of second and mixed types, Table III and Fig. 6B and D), and, in the third, the abnormalities were nonspecific (cf. Case 4, Table III and Fig. 6M). Although, in this series, there was good agreement between the electrocardiographic and necropsy diagnoses, it is clear that (1) some coronary patterns of recent myocardial infarction are caused by other lesions, and (2) some recent myocardial infarctions are overlooked in the electrocardiogram. The electrocardiogram is, after all, only part of the armamentarium of the clinician, and reliance entirely upon it for even this condition is not justifiable either in the positive or the negative sense. Absence of the pattern does not exclude the lesion if the clinical manifestations are diagnostic. A positive pattern should be viewed in the light of the clinical picture in order to exclude the possibility of other diseases which can produce a similar pattern. When there is doubt, positive evidence should outweigh negative evidence.

Of the old, healed myocardial infarcts which were found at necropsy (Table IV), only one was diagnosed in the electrocardiogram and then was wrongly located (cf. Case 2, anterior wall infarct, Table III and Fig. 6G). In the other 6, either left ventricular preponderance (cf. Cases 1 and 2, of second and mixed types, Table III and Fig. 6B and C) or nonspecific abnormalities (cf. Cases 1, 2, 3, and 6, Table III and Fig. 6J, K, L, and O) were found, with nothing to suggest the infarction. This is in sharp contrast with myocardial infarction of recent origin. It is for this reason that we have made it a practice to separate recent from old infarction. Little is lost in this lack of ability to diagnose old infarction, for, unlike recent infarction, its presence does

TABLE III  
SUMMARY OF CASES IN WHICH THERE WERE DISCREPANCIES

ECG. PATTERN (FIG. NO. WHERE ILLUSTRATED)	TOTAL NO. OF CASES	NO. OF DISCREPANCIES	INADEQUATE ECG. DATA	AGE	SEX	CHIEF CLINICAL FINDINGS	BODY WEIGHT KILOGRAMS	HEART WEIGHT GRAMS	LEFT VENT. THICKNESS, CM.	RIGHT VENT. THICKNESS, CM.	GROSS ANATOMY	MICROSCOPIC ANATOMY	NATURE OF DISCREPANCY
Within Normal Limits. (6A)	8	1	Single record	82	M	Diabetes mellitus	65	330	1.4	0.1	Coronary sclerosis; myocardial fibrosis; arteries rigid and in some areas almost occluded.	Fibers large and pale; increase in connective tissue.	For this age ECG is normal; however, there is a Q <sub>3</sub> and a tendency to low voltage; no evidence of left ventricular preponderance.
Left Ventricular Preponderance Without Infarction.	33	3											
First Type.	6	0											
Second and Mixed Types.	26	3											
Case 1. (6B)				56	M	Congestive heart failure, B.P. 130/80	50	500	1.2	0.1 to 0.4	Marked coronary sclerosis; old and recent infarct of apical, lower septal, and lower ant. wall of left ventricle. Moderate pulmonary emphysema.	Marked necrobiotic changes in muscle fibers; marked increase in connective tissue.	ECG shows no evidence of old infarct; recent one occurred after ECG taken. However, diagnosis of left ventricular preponderance fits.

Case 2. (6C)	Only CF <sub>2</sub>	M	Epigastric and precordial pain. B.P. 190/120	66	800	2.0	0.3	Coronary sclerosis with severe narrowing of left descending branch; old organizing infarct at apex.	Necrotic fibers, leucocytic infiltration, fibrosis.	No ECG evidence of organizing infarct at apex. Left ventricular preponderance fits.
Case 3. (6D)	Single record; only CF <sub>2</sub>	F	Severe chest pain. B.P. 140/85	104	375	1.0	0.1	Recent septal infarct; old infarct at apex of left ventricle with aneurysm.	Necrosis in septal wall; many small vessels thrombotic; a few foci of extensive fibrosis.	Changes are result of chronic coronary insufficiency. Record made within 24 hours of death; single records often fail to reveal classical picture. Repeat record requested, but patient died.
Concordant Type.	1	0								
Right Ventricular Preponderance Without Infarction.	12	0								
Combined Ventricular Strain Without Infarction. (6E)	3	1	Chronic bronchitis; bronchopneumonia	50	300	1.0	0.3 to 0.8	Patent coronary arteries; enlarged pulmonary conus; emphysema	Myofibrils somewhat thickened.	ECG and necropsy show cor pulmonale; S <sub>1</sub> and S <sub>2</sub> indicative of left strain but this was not shown at necropsy.
Congenital Heart Disease.	3	0								
Recent Myocardial Infarction.	26	4								



Atypical patterns. (6I)	5	1	39	M	Polycneuritis; edema; ascites; peritonitis.	35	250	1.3	0.3	Brown atrophy of heart. Coronary arteries patent.	Granular and atrophic fibrils. Seattered connective tissue increase.	No infarct found at autopsy. Changes in ECG may be due to vitamin deficiency state.
Acute Diffuse Pericarditis Without Recent Myocardial Infarction.	3	0										
Acute Diffuse Pericarditis With Recent Myocardial Infarction.	2	0										
Acute Cor Pulmonale.	1	0										
Chronic Cor Pulmonale.	3	0										
Mitral P Wave.	11	0										
Cor Pulmonale P Wave	5	0										
Non-Specific Abnormalities.	60	9										
Case 1. (6J)			69	M	Congestive heart failure. B.P. 120/80	68	475	1.0 to 1.5	0.3 to 0.6	Marked coronary sclerosis; apex of left ventricle and septum show aneurysm.	Enlarged myofibrils; large areas replaced by hyaline connective tissue.	The ECG pattern does not fit with old healed myocardial infarction. Suggests right ventricular preponderance.

TABLE III—CONT'D

ECG. PATTERN (FIG. NO. WHERE ILLUSTRATED)	TOTAL NO. OF CASES	NO. OF DISCREPANCIES	INADEQUATE ECG. DATA	AGE	SEX	CHIEF CLINICAL FINDINGS	BODY WEIGHT KILOS	HEART WEIGHT GRAMS	LEFT VENT. THICKNESS, CM.	RIGHT VENT. THICKNESS, CM.	GROSS ANATOMY	MICROSCOPIC ANATOMY	NATURE OF DISCREPANCY
Case 2. (6K)			Single record, only CF <sub>2</sub>	57	F	Congestive heart failure. B.P. 158/100	55	350	1.5	0.5	Old posterior infarct; marked coronary sclerosis; healed en- docarditis of mitral and tricuspid valves.	Patchy fibrosis; enlarged my- ofibrils.	ECG shows no evi- dence of old infarct present at autopsy.
Case 3. (6L)			Single record	59	M	Rheumatic fe- ver, abdom- inal pain.	60	350	1.0	0.3 to 0.5	Old posterior wall in- farct. Mitral steno- sis. Moderate coro- nary sclerosis. Mul- tiple liver abscesses.	Increase fibrous tissue in post. wall. Myofibrils of right vent. swollen.	Digitalis contour in ECG, no evidence of old posterior wall infarct.
Case 4. (6M)			Single record, only CF <sub>2</sub>	65	M	Sudden collapse. Congestive heart failure.	64	350	1.2	0.3	Recent post. wall in- farct; marked coro- nary sclerosis. Pneumonia.	Neurotic fibers —posterior wall. Diffuse fibrosis.	Record taken at time of attack; this may explain failure of ECG to show in- farct. Patient died before repeat rec- ord could be taken.
Case 5. (6N)			Only CF <sub>2</sub>	32	M	Rheumatic heart disease. Conges. heart failure.	70	500	1.4	0.3	Healed endocarditis mitral and aortic valves with insuffi- ciency and stenosis. Patent coronary ar- teries.	Diffuse increase in connective tissue. En- larged myo- fibrils.	Depression of S-T, as- cribed to digitalis. No evidence of left or right ventricular strain.

Case 6. (6P)			73	M	Angina pectoris; pleural effusion.	N.G.	325	1.2	0.3	Carcinoma of lung extending into left auricular wall; old anterior wall infarct.	Dense connective tissue in region of infarct. Tumor cells in left auricle.	ECG fails to show evidence of old anterior wall infarct. If anything $Q_a$ would point to posterior wall infarction; invasion of heart by tumor may account for changes.
Case 7. (6P)		Single record, no CF <sup>27,4</sup>	5	M	Abdominal pain; bloody stools; albuminuria; B.P. 190/140	20	125	--	--	Acute peritonitis and enteritis. Hypoplasia of right kidney. Hypertrophy of left ventricle.	No microscopic observation.	No ECG evidence of left ventricular preponderance found at autopsy.
Case 8. (6Q)		Single record, only CF <sub>5</sub>	52	F	Uremia. Congestive heart failure. B.P. 228/112	N.G.	825	2.1	0.5	Plaques in coronary arteries. Marked hypertrophy of heart. Nephrosclerosis.	Diffuse increase in connective tissue.	ECG shows only left axis shift and nothing to indicate hypertrophy found at autopsy.
Case 9. (6K)		Single record, only CF <sub>5</sub>	42	M	Rheumatic heart disease. Congestive heart failure.	N.G.	500	1.7	0.3	Acute vegetative endocarditis; old mitral and aortic endocard.	Swollen granular fibrils; scattered leucocytes and lymphocytes.	Left axis shift with low voltage. No evidence of hypertrophy in ECG.
Total	170 patterns in 149 cases with 18 exceptions											

N.G. = Not given.

TABLE IV  
THE ELECTROCARDIOGRAPHIC PATTERNS WITH DIFFERENT TYPES OF NECROPSY CHANGES

AUTOPSY OBSERVATIONS	NUMBER OF CASES	ELECTROCARDIOGRAPHIC PATTERN	
		AGREE	DISAGREE (FIG. NO. SHOWING ILLUSTRATION)
Hypertrophy of Left Ventricle	24	21	3 1st showed right axis shift and non-specific abnormality (6P). 2nd showed left axis shift and non-specific abnormality (6R). 3rd was within normal limits (6A).
Hypertrophy of Right Ventricle	8	7	1 It showed combined right and left ventricular strain (6E).
Hypertrophy of Both Left and Right Ventricles	19	15	4 1st showed left axis shift and diffuse pericarditis. 2nd showed left axis shift and non-specific abnormality (6Q). 3rd showed no axis shift and non-specific abnormality (6N). 4th showed left axis shift and non-specific abnormality (6R).
Congenital Heart Disease	4	3	1 It showed only right ventricular preponderance.
Recent Myocardial Infarction	25	22	3 2 showed only left ventricular preponderance (6R & D). 1 showed only nonspecific abnormality (6M).

Old Healed Myocardial Infarction	7	1 (6G)	6 2 showed only left ventricular preponderance (6B & C). 4 showed only nonspecific abnormality (6J, K, L & O).
Recent Diffuse Pericarditis Without Recent Myocardial Infarction	3	3	0
Recent Diffuse Pericarditis With Recent Myocardial Infarction	4	2 (seen in the S-T stage)	2 (seen in T stage) Gave no evidence of complicating pericarditis.
Acute Cor Pulmonale (Massive Pulmonary Embolism)	3	1	2 1st showed a posterior wall infarct pattern (6H). 2nd showed only intraventricular block of the 2nd indeterminate type (7B).
Chronic Cor Pulmonale	8	4 3 showed cor pulmonale P wave. 1 showed auricular fibrillation.	4 They showed no cor pulmonale P wave or auricular fibrillation.
Hypertrophy and (or) Dilation of Left Auricle	10 8 rheumatic mitral. 1 congenital heart. 1 arteriosclerotic.	8 6 rheumatic { 4 mitral P wave, 2 auricular fibrillation 1 congenital—P pattern not entirely typical. 1 arteriosclerotic—auricular fibrillation.	2 Both rheumatic—P wave pattern not abnormal.
Hypertrophy and (or) Dilation of Right Auricle	2 1 chronic cor pulmonale. 1 recent myocardial infarct.	2	0
Hypertrophy and (or) Dilation of Left and Right Auricles	10 9 rheumatic { 1 mitral. 8 mitral and tricuspid. 1 arteriosclerotic	10 9 rheumatic { 7 mitral P wave, 2 auricular fibrillation. 1 arteriosclerotic—auricular fibrillation.	0

not affect the immediate prognosis, and it usually requires less stringent management.

It was surprising that the electrocardiographic pattern of chronic coronary insufficiency did not occur in this series, except for the case in which there was an old, healed myocardial infarct. Examination of the necropsy records revealed 54 cases of coronary sclerosis without infarction; in all but four there was myocardial fibrosis of a degree which corresponded to the extent of the coronary sclerosis. In 5, complete closure of one of the main branches of the coronary vessels was found. In the 50 cases of coronary sclerosis and myocardial fibrosis the following were the electrocardiographic changes:

(a) In 9, intraventricular block (in most of these there was marked myocardial fibrosis).

(b) In 21, ventricular strain patterns, all with ventricular hypertrophy; 17 of these could be explained as a result of associated valvular lesions, pulmonary disease, or systemic hypertension, whereas, in 4, the hypertrophy of the left ventricle was unexplained unless it could be attributed to the coronary sclerosis and the consequently reduced blood supply.<sup>16, 17</sup>

(c) In 20, nonspecific abnormalities.

These observations are significant because they indicate that the electrocardiogram usually does not show specific patterns in coronary sclerosis; this is an observation which we,<sup>18</sup> as well as many others, have noted previously. Nonspecific abnormalities in the arteriosclerotic age group which are not otherwise explained should therefore be considered as evidence of coronary sclerosis.

The absence of the specific coronary pattern in coronary sclerosis and myocardial fibrosis, as well as in most instances of old, healed myocardial infarction, supports our contention<sup>4</sup> that the specific S-T-T changes are primarily the result of injury to living muscle tissue, and hence evidence of coronary insufficiency.

Two of the cases of infarction deserve further mention, namely, the one of old, healed infarction, the other of recent infarction. The infarct in both cases was located on the lateral wall of the left ventricle. In the former (cf. Case 2, Table III and Fig. 6G), the limb leads showed the anterior wall pattern. In the second (Fig. 7A), the limb leads showed the anterior wall pattern but the chest leads were normal, so that the record was regarded as showing an atypical coronary contour. In neither case was the pattern like that described by Wood, et al.,<sup>19</sup> as characteristic of lateral wall infarction, so that the interpretation of these authors may be questioned.

*Acute Diffuse Pericarditis.*—There were 5 cases in which this disease was diagnosed in the electrocardiogram. In 3 it was thought to be associated with recent myocardial infarction, and in 2 it was not (Table

II). In all 5 cases the lesions diagnosed in the electrocardiogram were found at autopsy. No other cases of acute diffuse pericarditis without recent myocardial infarction were found at necropsy. However, 5 cases of old, healed, diffuse pericarditis, without infarction, were encountered. As expected, in one of these there was a characteristic pattern, and, in another, there were suggestive changes; all, however, were classed as nonspecific abnormalities.

By contrast, in 2 of the 4 cases of acute diffuse pericarditis *with* recent myocardial infarction, there was electrocardiographic evidence of the recent myocardial infarction only (Table IV). These lesions were in the T stage, whereas those which were correctly diagnosed were in the S-T stage.<sup>8</sup>

This substantiates the deduction that acute diffuse pericarditis can be diagnosed in the electrocardiogram.<sup>8</sup>

*Acute Cor Pulmonale.*—In the one case in which this diagnosis was made from the electrocardiogram, autopsy revealed a recent, massive, pulmonary embolism (Table II). Recent, massive, pulmonary embolism was present at necropsy in 2 other cases in this series (Table IV). In one, the electrocardiogram showed a typical posterior wall infarction pattern (cf. Table III and Fig. 6H). In this case there was no S<sub>1</sub>, Lead II resembled Lead III instead of Lead I, and T was upright instead of inverted in CF<sub>2</sub>.<sup>20</sup> In the second case (Fig. 7B) there was intraventricular block of the second indeterminate (or S) type,<sup>21</sup> which is not uncommon but not diagnostic of recent pulmonary embolism. The absence of the characteristic changes in the electrocardiogram in some cases of pulmonary embolism agrees with our previous observations.<sup>10</sup>

*Chronic Cor Pulmonale.*—In the three cases in which this diagnosis was made from the electrocardiogram (Table II), necropsy revealed right ventricular hypertrophy due to pulmonary emphysema. However, 5 other cases of pulmonary emphysema and right ventricular hypertrophy were found at necropsy (Table IV). In two of these there were nonspecific abnormalities and right axis shift; in two, intraventricular block of the second indeterminate (or S) type; and, in one, left ventricular preponderance (associated with hypertension). One of these patients had had auricular fibrillation, and in the others no cor pulmonale P pattern occurred. The ability to diagnose this condition is thus limited, but the characteristic pattern is diagnostic.

*P-wave Patterns.*—There were eleven cases in which the P pattern was of the *mitral P type* (Table II). In all of these it was presumed that the left auricle was under strain because of rheumatic mitral stenosis. In all eleven, necropsy revealed a rheumatic lesion of the mitral valve, with stenosis. In six of these cases there was involvement (dilatation and/or thickening) of the left auricle and not of the right; in the other five there was involvement of both auricles, but because of the mitral involvement the strain was presumed to be domi-

nant in the left auricle. Apparently, then, the generally accepted significance of the mitral P pattern is borne out in this series.

At necropsy, 4 additional instances of left auricular hypertrophy and/or dilatation and 5 more cases of such involvement of both auricles were encountered (Table IV). In 6 of these additional 9 cases auricular fibrillation was present (which is a common equivalent of the mitral P wave). In one of these cases, associated with congenital heart disease, the P pattern, although definitely abnormal, was not characteristic of the mitral type. In the last two cases there were no P wave abnormalities: one was a case of calcific aortic stenosis, and the other was a case of healed mitral endocarditis and massive pulmonary embolism.

Incidentally, the commonest cause of combined right and left auricular strain was the simultaneous presence of mitral and tricuspid valvular involvement (Table IV). In these instances the mitral lesion was apparently the more significant, for the mitral P wave pattern occurred in the majority. Another interesting observation was the fact that in the two cases of arteriosclerosis auricular fibrillation was present, whereas in only 4 out of 17 cases of rheumatic heart disease did this arrhythmia occur.

In five cases there was a *cor pulmonale P wave* (Table II), and in all of them there was necropsy evidence of chronic pulmonary abnormalities which might place a strain on the right auricle. However, in only two of the cases was the right auricle described in the autopsy protocol as being thickened. This accords with a previous report.<sup>22</sup> However, in the two cases (Table IV) in which the right auricle was reported dilated and/or thickened, without involvement of the left auricle, the *cor pulmonale P* pattern was present. This is contrary to a previous report.<sup>23</sup> It would appear, therefore, that this pattern may be of value in detecting strain on the right auricle.

This study shows that the contour of the P wave may be of value in locating the dominant strain in the auricles in a manner similar to that employed with QRST for ventricular strain.

*Nonspecific Abnormalities.*—In 60 cases the abnormalities were regarded as nonspecific. This, of course, includes lesions which are not expected to give a specific pattern, instances in which lesions that are expected to give specific patterns failed to do so, and lesions which, as our knowledge advances, may come to have specific patterns associated with them. In 9 of the 60 cases of nonspecific abnormalities there were lesions at necropsy which should have produced specific electrocardiographic patterns. These are detailed in Table III and illustrated in Fig. 6J to R. They have been discussed earlier in this report, and are mentioned here again only to emphasize that heart strain and recent myocardial infarction may occasionally not be revealed in the electrocardiogram, and that old, healed myocardial infarcts often do not produce specific electrocardiographic patterns. This is true also of coronary sclerosis and myocardial fibrosis.

## SUMMARY AND CONCLUSIONS

1. The electrocardiographic patterns and anatomic abnormalities in 149 consecutive autopsy cases were compared.
2. The criteria of normal and abnormal electrocardiograms are described, as well as the 12 specific electrocardiographic patterns which were encountered in this series.
3. The criteria employed in the electrocardiographic diagnosis proved to be accurate.
4. The recognition of definite patterns increases the diagnostic value of the electrocardiogram.
5. An abnormality in the electrocardiogram can be considered as objective evidence of a cardiac abnormality, but does not necessarily reveal the clinical status of the heart. The fact that the electrocardiogram is normal cannot be considered as objective proof that the heart is normal in all instances.
6. In cases of combined hypertrophy of the right and left ventricles, the electrocardiogram usually reflects only the predominant ventricular strain. Right ventricular preponderance is more often correctly diagnosed and less often overlooked than left ventricular preponderance. Marked hypertrophy, especially if both ventricles are involved, may be present without electrocardiographic evidence of ventricular strain.
7. Cases of old, healed, anterior wall infarction may be indistinguishable from cases of left ventricular hypertrophy without myocardial infarction. Conversely, left ventricular hypertrophy may give rise to an electrocardiographic pattern which is suggestive of recent anterior wall infarction.
8. The electrocardiographic pattern of congenital heart disease is diagnostic.
9. The patterns associated with recent myocardial infarction are significant, although errors both of commission and omission occur. These errors are less likely to occur when chest leads and serial curves are obtained.
10. Old, healed, myocardial infarction commonly fails to produce any characteristic electrocardiographic pattern.
11. Coronary sclerosis and myocardial fibrosis seldom give rise to any particular pattern in the electrocardiogram.
12. The electrocardiographic localization of myocardial infarction was found to be correct in this series except in one case of old, healed infarction.
13. In the two cases of lateral wall infarction which were encountered, there were anterior wall patterns in the limb leads.
14. Recent, diffuse pericarditis can be recognized in the electrocardiogram, and this is possible in the presence of associated conditions which tend to mask the pattern.

15. The patterns of acute cor pulmonale are diagnostic, but extensive, massive, pulmonary embolism may occur without these patterns. An instance of massive pulmonary embolism which closely imitated the pattern of recent posterior wall infarction is cited.

16. Chronic cor pulmonale may produce a characteristic electrocardiographic pattern which is diagnostic.

17. The cor pulmonale P wave pattern occurs in instances of dominant right auricular dilatation and/or hypertrophy, but this is not always true.

18. The mitral P wave pattern is indicative of left auricular involvement. It is an important diagnostic sign, and, in the present series, constituted electrocardiographic evidence of rheumatic heart disease.

19. The results of this study indicate that the electrocardiogram may be utilized to diagnose cardiac abnormalities and to suggest the presence of particular types of heart disease. If a conservative approach is made, the diagnostic value of the electrocardiogram justifies its present use, and this should expand as experience and critical analyses are continued.

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## DISSECTING ANEURYSM OF THE AORTA

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A DISSECTING aneurysm is the lesion produced by penetration of the circulating blood for a varying distance between the layers of the wall of a vessel.<sup>1</sup> Although Fernellius<sup>2</sup> was the first to observe an aortic aneurysm and Vesalius<sup>3</sup> the first to diagnose one, it was not until several centuries later that Maunoir<sup>4</sup> clearly suggested that there may be dissection of the arterial coats by the blood. Cases of long standing, in which the blood circulates through the new sac, were first reported by Shekelton,<sup>5</sup> but Laennec<sup>6</sup> was the earliest writer to use the term in a publication. Elliotson<sup>7</sup> gave a clear and correct description of this condition, and Pennock,<sup>8</sup> in reporting a case of long standing, demonstrated that the dissection takes place between the laminae of the media. Rokitsansky<sup>9</sup> differentiated simple rupture of the aorta from dissecting aneurysm. It remained for Peacock<sup>10</sup> to clarify the state of knowledge on this most unusual condition.

He described,<sup>11</sup> among his many cases,<sup>12</sup> three stages in the development of a dissecting aneurysm: (1) the incipient stage, in which there are rupture or destruction of a part or the whole of the internal coats of the vessel and extravasation of blood to a limited extent between the external and middle coats, or more probably in the laminae of the latter; (2) the early stage of a fully formed dissecting aneurysm, in which, in addition to the internal rupture, there is more extensive extravasation of blood in the coats of the vessel, separating the middle from the external tunic, or in the laminae of the middle coat for a variable distance along the aorta, and not infrequently along its primary branches, usually with external rupture into some of the adjacent cavities; and (3) the advanced stage, in which there is an opening through the internal coats leading into a sac situated within the tunics which extends along the course of the vessel and is lined by a distinct membrane very similar to the natural lining membrane of the arteries. Among the 80 cases referred to by Peacock<sup>13</sup> is the first dissecting aneurysm diagnosed during life.

Fagge<sup>14</sup> stated that if, after the first shock of the formation of the aneurysm, the patient returned to a tolerable state of health and survived for a considerable length of time, a lower communication between the sac and the aorta and some large vessel may develop. The possibility of "complete healing," with the new channel taking up part of the function of the aorta, was emphasized by Bostrom.<sup>15</sup> Adami<sup>16</sup> dealt only with cases of long standing, and suggested the term "arrested"

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dissecting aneurysm in place of "healed." The important conclusions of Floeckemann,<sup>17</sup> that the dissection is probably not conditioned by disease of the vessel, and only in exceptional cases by trauma, and that, consequently, the preliminary intimal rupture is caused by overstretching of the aorta as a result of forcible action of a hypertrophied and competent left ventricle, have been generally accepted.

An outstanding contribution to this subject is that of Shenan;<sup>1</sup> he analyzed all of the material to 1933 (300 cases, including 17 of his own).

The present analysis of the 112 adequately studied cases<sup>18</sup> of dissecting aortic aneurysm reported since 1933 indicates further that this syndrome, as pointed out mainly by Peacock and Shenan, is not a uniform clinical entity. Such cases do not occur frequently, and the clinical diagnosis is often difficult to establish. The rarity of such aneurysms at even large institutions may well be emphasized; only 19 cases (0.14 per cent) have been noted in 14,160 autopsies in the period from 1929 to 1941 at the Cook County Hospital. The incidence has been similarly low at the Charity Hospital of Louisiana, at New Orleans,<sup>19</sup> and the Massachusetts General Hospital.<sup>20</sup>

This report is based on the 19 patients with dissecting aneurysm of the aorta who came to autopsy at the Cook County Hospital. Although the condition was suspected in some of the cases, mainly in the few in which there was an acute onset, the diagnosis was not established clinically in any instance. There were 13 males (5 white and 8 colored) and 6 females (2 white and 4 colored); their ages varied from 22 to 70 years, with an average age of 51.8 years.

It has been the custom to classify the dissections into two types, namely, those of recent origin and the old "arrested" or "healed" aneurysms. However, a review of the literature and the analysis of the present 19 cases led to a somewhat different viewpoint. There were (1) old dissections which were (a) "silent" or (b) active, and (2) recent dissections which were (a) typical or (b) atypical. Such a viewpoint, bearing in mind that it is possible to have four completely different clinical pictures of dissecting aneurysm of the aorta, may help in the diagnosis and prognosis of this condition. The main reason for expressing this view is the fact that the average duration of life with the old dissections was 3 years, whereas, with the recent ones, it was only 17.6 days.

#### OLD, "SILENT" DISSECTIONS

In these 12 cases there was a gradual onset of symptoms and signs of congestive heart failure. None of the 12 patients had a history of excruciating pain in the chest radiating into the neck, the back, or the abdomen. In four of these cases, in addition to the congestive failure, the physical and roentgenologic observations led to a diagnosis of syphilitic aortic aneurysm. The outstanding feature of these old, "silent" dissections was the intractable heart failure, and the following cases illustrate the important abnormalities.

CASE 2.—L. F., a white man, 55 years old, first entered the hospital on February 16, 1930. He complained only of dyspnea, cough, and weakness of two months' duration. Physical examination revealed a very dyspneic patient who had a blood pressure reading of 240/160, impaired resonance and moist râles at the bases of both lungs, and a transverse cardiac measurement of 18 cm. The only laboratory data of note were the Wassermann reactions on the blood and spinal fluid, both of which were moderately positive (2 plus). With absolute rest in bed and digitalis he responded slowly, but not well, and he left the hospital at his own request on March 5, 1930. He re-entered April 30, 1930, complaining of marked weakness, a loss of 20 pounds in weight, and hemoptysis, in addition to dyspnea and cough. The physical signs were completely altered. There was a difference in the blood pressure in the two arms; on the left it was 148/52, and, the right, 122/52. There was a marked difference in the radial pulses; the right was scarcely palpable, and the left was water-hammer in character. The heart was enlarged (transverse diameter, 22 cm.), and systolic and diastolic murmurs were audible over the aortic area. A pistol-shot sound was heard over the femoral arteries. Dullness and moist râles were present over the bases of both lungs. The Wassermann reactions on both the blood and spinal fluid were again moderately positive. Roentgenologic examination of the chest, which had previously revealed only an enlarged heart, now showed a diffuse enlargement of the aortic shadow. The symptoms became steadily worse, and the patient attempted suicide by cutting his wrists. Death occurred May 20, 1930, as a result of infection of the self-inflicted lacerations. Autopsy (by Dr. Phillip Shapiro) revealed (1) an ancient dissecting aneurysm of the arch of the aorta, with rupture two fingerbreadths above the valve and return rupture at the junction of the transverse and descending portions, (2) a double tube in the arch of the aorta which extended into the innominate and the left common carotid arteries, (3) atheromatosis of the aorta, (4) eccentric hypertrophy of the heart, which weighed 700 grams, with dilatation of the left ventricle, (5) chronic passive congestion of the lungs, liver, kidneys, spleen, and gastrointestinal mucosa, and (6) acute infectious splenic tumor.

CASE 3.—B. J., a white man, 50 years old, first entered the hospital February 15, 1930, complaining of dyspnea of one year's duration. The only abnormalities were moist râles at the bases of both lungs, a blood pressure of 260/150, a transverse cardiac measurement of 15 cm., and a rough systolic murmur at the apex. He responded slowly and poorly to treatment with digitalis. Between the first admission and his final entrance into the hospital 19 months later, he was hospitalized on six other occasions, each time for a longer stay. He was markedly decompensated and edematous when he re-entered for the last time on October 7, 1931. Physical examination revealed a very cyanotic, orthopneic, and poorly nourished man. The blood pressure in both arms was 210/120. The transverse diameter of the heart was enlarged to 19 cm., and there was an irregularity of rate and rhythm. General anasarca was present. Laboratory examination was negative except that the urine showed 2+ albumin and many hyaline casts. He grew steadily worse, but with absolute rest in bed he lived until February 16, 1932, three years after the onset of the first symptom and two years after he was first hospitalized. Autopsy (by Dr. Victor Levine) revealed (1) an ancient dissecting aneurysm of the descending aorta and marked atheromatosis of the aorta, (2) thrombosis of the lower end of the newly formed lumen of the aorta, (3) an ancient fibroplastic deformity of the aortic valve, with moderate stenosis and insufficiency, and a recent verrucous endocarditis of the mitral valve, (4) marked eccentric hypertrophy of the heart, which weighed 540 grams, (5) chronic passive congestion of the lungs, kidneys, and spleen, (6) chronic passive congestion of the liver, with early cardiac cirrhosis, (7) arteriosclerosis of the kidneys, and (8) hydrothorax, hydropericardium, and ascites.

## OLD, "ACTIVE" DISSECTIONS

There were four patients with old dissections, but the lesions were "active" throughout. Except for the history, the clinical manifestations varied little from those in the cases of old, "silent" dissections. The history was one of repeated attacks of pain in the chest, neck, and back over a period of weeks or months, until a final excruciating attack was experienced.

CASE 13.—M. P., a colored woman, 50 years of age, entered the hospital October 15, 1934. She stated that she was well until six months before entry, when she began to have severe attacks of pain in the front of the chest that went up into the neck and through to the back. At first the attacks lasted only a few minutes, but each successive one lasted a little longer, and she became short of breath. Six hours before admission she experienced an attack of excruciating pain in the chest that radiated in the manner described. The pain persisted and dyspnea became very marked. On physical examination she appeared very ill. The blood pressure was 152/64 in both arms. The left border of the heart was 13 cm. from the midsternal line, and loud, rough, systolic and diastolic murmurs were audible at the aortic area. The pulse was water-hammer in character. Laboratory examination was negative. Her pain increased; she grew worse steadily, and died October 18, 1934. Autopsy (by Dr. Frank B. McJunkin) revealed (1) a dissecting aneurysm (not recent) of the aorta, with extension of the dissection into both common iliac arteries and the innominate artery, and rupture into the pericardial sac, (2) hemopericardium (250 c.c.), (3) atherosclerosis of the aorta, (4) bilateral hydrothorax, and (5) passive congestion of the viscera.

CASE 14.—A. C., a white woman, 69 years old, entered the hospital June 30, 1937. In February, 1937, she had an attack of "grippe," and was then well until April, 1937, when, on trying to open an umbrella against the wind, she had an attack of severe pain in the chest and a sensation as if she were choking to death. She had four similar attacks that day, and another at 4 A.M. the next day which was brought on by arising. Thereafter she stayed in bed under medical care, but the attacks continued, and the pain radiated into the neck and the back. She became increasingly short of breath. Physical examination on admission to the hospital, three months after the initial attacks of pain, revealed a very acutely ill woman. The blood pressure in both arms was 140/60. There were moist râles at the bases of both lungs. The apex beat was diffuse, heaving, and irregular. The left border of the heart was 15 cm. from the midsternal line. Systolic thrills were palpable over the apex and the base of the heart, and the heart tones were harsh. A rough systolic murmur was audible over the apex. The rate and rhythm were grossly irregular. She became steadily worse, and died July 26, 1937. Autopsy (by Dr. Ben W. Lichtenstein) revealed (1) a dissecting aneurysm (not recent) of the ascending portion and arch of the aorta, with rhexis at three points, (2) slight hypertrophy of the heart, which weighed 350 grams, (3) severe atherosclerosis of the aorta, (4) bilateral hydrothorax, and (5) passive congestion of the lungs, liver, and spleen.

## RECENT DISSECTIONS

Three patients had recent dissecting aneurysms of the aorta, but in only two was there the so-called typical clinical picture. One patient had excruciating chest pain, and the other collapsed suddenly. In both cases the clinical diagnosis was coronary thrombosis, the condition with

TABLE  
ESSENTIAL DATA ON NINETEEN AUTOPSY

CASE	SEX	COLOR	AGE	TYPE	DURATION	MURMURS	EKG.	SYPHILIS
1	M	C	56	Old silent	5 years	None	LAD*	-
2	M	W	55	Old silent	6 months	Systolic-diastolic at aortic area	LAD	+
3	M	W	50	Old silent	3 years	Systolic at apex	A.F.†	-
4	M	W	51	Old silent	2 years	Systolic at apex	LAD, T <sub>1</sub>	-
5	M	C	50	Old silent	2½ years	Systolic-diastolic at apex and base	LAD	-
6	M	C	70	Old silent	1 year	Systolic-diastolic at apex and base	LAD	-
7	M	C	51	Old silent	1 month	Systolic-diastolic at apex	LAD	-
8	M	C	31	Old silent	3 years	Systolic-diastolic at apex and base	BBB‡	-
9	M	C	62	Old silent	2 years	Systolic-diastolic at apex and systolic at base	A.F.	+
10	F	C	55	Old silent	5 years	Systolic-diastolic at base	LAD	-
11	F	C	53	Old silent	10 years	Systolic-diastolic at base	LAD	-
12	M	W	52	Old silent	3½ years	Systolic at apex and base	LAD	+
13	F	C	50	Old active	6 months	Systolic-diastolic at base	LAD	-
14	F	W	69	Old active	4 months	Systolic at apex	A.F.	-
15	F	C	40	Old active	?	Systolic-diastolic at aortic area	None	-
16	M	C	67	Old active	?	None	None	-
17	M	C	67	Recent typical	36 days	Systolic at apex	LAD, T <sub>1</sub> , T <sub>2</sub>	-
18	F	W	55	Recent typical	6 days	Systolic at aortic area	None	-
19	M	W	22	Recent atypical	11 days	Systolic-diastolic at apex and base	LAD	-

\*Left Axis Deviation.

†Auricular Fibrillation.

‡Bundle Branch Block.

## I

## CASES OF DISSECTING ANEURYSM OF THE AORTA

CLINICAL DIAGNOSIS	AUTOPSY FINDINGS		
	HEART DISEASE	HEART WEIGHT	CAUSE OF DEATH
Hypertensive Heart Disease	Hypertensive	825 Gm.	Rupture of ascending aorta
Hypertensive and Luetic Heart Disease and Aneurysm	Hypertensive and Luetic Aortitis	700 Gm.	Septicemia
Hypertensive Heart Disease	Hypertensive and Coronary	540 Gm.	Thrombosis of newly formed aorta
Hypertensive Heart Disease	Hypertensive	890 Gm.	Rupture of ascending aorta
Luetic Heart Disease	Hypertensive and Coronary	690 Gm.	Rupture of ascending aorta
Multiple Aneurysmal Dilatation of Aorta	Coronary and Hypertensive	510 Gm.	Empyema
Hypertensive Heart Disease	Hypertensive	565 Gm.	Congestive Heart Failure
Luetic Heart Disease	Hypertensive	810 Gm.	Rupture of ascending aorta
Luetic Heart Disease	Luetic, Hypertensive, and Coronary	625 Gm.	Rupture of ascending aorta
Luetic Heart Disease	Hypertensive	450 Gm.	Rupture into pericardial sac
Hypertensive and Luetic Heart Disease	Coronary and Hypertensive	480 Gm.	Pulmonary embolism
Aortic Aneurysm	Hypertensive and Luetic	720 Gm.	Congestive Heart Failure
Luetic Heart Disease	Hypertensive and Coronary	500 Gm.	Rupture into pericardial sac
Coronary Heart Disease	Coronary and Hypertensive	350 Gm.	Rupture, ascending and arch of aorta
Luetic Heart Disease	Hypertensive	550 Gm.	Rupture into pericardial sac
Left Lower Lobar Pneumonia	Hypertensive and Coronary	700 Gm.	Rupture into pericardial sac
Coronary Thrombosis	Hypertensive and Coronary	550 Gm.	Rupture of ascending aorta
Coronary Thrombosis	Hypertensive	450 Gm.	Rupture into pericardial sac
Aortic and Mitral Endocarditis, with rupture of aortic leaflet	Hypertensive	590 Gm.	Multiple ruptures (5) of aorta

which dissecting aneurysm is most commonly confused. The two cases were as follows:

CASE 17.—G. A., a colored man, 67 years old, entered the hospital November 20, 1932. He had been well until the day before admission, when he was suddenly seized with excruciating pain in the epigastric region. He vomited twice at the onset, but got no relief. The pain persisted. The only other significant fact in the history was that, 3 years earlier, one of his legs had been amputated because of gangrene secondary to atherosclerotic occlusion of the popliteal artery. The blood pressure was 184/104 in both arms, the left border of the heart was 11 cm. from the mid-sternal line, and the heart tones were soft and muffled; a rough, blowing, systolic murmur was audible over the base of the heart. The percussion note over the base of the left lung was flat, and no breath sounds could be heard over the area of flatness. Roentgenologic examination of the chest on November 23 showed a widening of the aortic arch suggestive of aneurysm. With absolute rest in bed the pain disappeared, and he seemed to be recovering, but died suddenly on December 16, 1932, twenty-six days after the onset of the severe pain. Autopsy (by Dr. Victor Levine) revealed (1) a recent dissecting aneurysm of the aorta, with rupture at the level of the obliterated ductus arteriosus and just above the bifurcation, (2) perforation of the dissecting aneurysm near the attachment of the ductus arteriosus into the periaortic and mediastinal fat, (3) extension of the hemorrhage from the mediastinal fat into the left pleural cavity, with the formation of an encapsulated hematoma containing 1000 c.c. of liquid blood, (4) marked eccentric hypertrophy of the heart, which weighed 550 grams, (5) marked sclerosis of the base of the aortic valve, (6) moderate sclerosis of the aorta and the coronary and iliac arteries, and focal medionecrosis of the aorta, (7) atheromatosis of the mesenteric and subclavian arteries, and (8) arteriosclerosis of the kidneys, with cyst formation.

CASE 18.—L. S., a white woman, 55 years old, entered the hospital April 11, 1940. While at work on the morning of the day of entry, she suddenly collapsed and had involuntary urination and defecation. On entrance, several hours later, it was noted that she spoke with difficulty and could not move either the upper or lower extremity on the right side. She had no pain. Physical examination revealed an ashen color of the face, a questionable blood pressure reading of 110/70, no perceptible pulse on the right and a palpable pulse on the left side, extension of the left border of the heart 12 cm. from the midsternal line, faint heart tones, with a rough systolic murmur over the aortic area, and paresis of the right upper and lower extremities. By the third hospital day she had improved considerably; she had a full pulse in both extremities, normal speech, and a complete return of function in the right arm and leg. The patient was feeling good, but died suddenly on the fifth hospital day, April 16, 1940. Autopsy (by Dr. William P. Mavrelis) revealed (1) a dissecting aneurysm of the arch and descending and abdominal aorta, (2) rupture of the ascending arch, with a hemopericardium of 250 c.c. of blood tinged fluid and 450 grams of clotted blood, (3) extension of the dissecting aneurysm into the innominate, the left common carotid, and both the subclavian and iliac arteries, (4) thrombosis of the dissecting sacs of the innominate and left common carotid arteries, with compression of their lumina, (5) aneurysmal outpouching of the ascending arch of the aorta, (6) marked eccentric hypertrophy of the heart, which weighed 450 grams, (7) marked coronary sclerosis, (8) marked passive congestion of the liver and kidneys, and (9) benign nephrosclerosis.

In addition to the absence of pain and collapse and the comparative youth of the patient, the other case of recent dissection was atypical in other respects.

CASE 19.—L. S., a 22-year-old white man, was admitted to the hospital January 21, 1940. A week before entrance he contracted an acute upper respiratory infection which was accompanied by a persistent, productive cough. On the day before

admission, while sitting up in bed, he suddenly developed severe shortness of breath and extreme weakness. Even in the upright position he could hardly breathe. There was no pain or hemoptysis. The history was negative for previous dyspnea, palpitation, and edema, but it was later learned that his brother, 27 years old, was under treatment at another hospital for "high blood pressure" and "heart trouble." The patient was extremely dyspneic and orthopneic, and severely ill. The blood pressure in both arms was 114/48. The left border of the heart was 13 cm. from the midsternal line. Loud, harsh, systolic and diastolic murmurs were audible at the apex and base of the heart. A systolic thrill was palpable over the right carotid artery. He had a very stormy course, heavy doses of morphine notwithstanding, and died four days after admission to the hospital (January 25, 1940). Autopsy (by Dr. A. C. Bach) revealed (1) a dissecting aneurysm, with multiple tears of the ascending portion, the arch, and the abdominal portions of the aorta, (2) marked eccentric hypertrophy of the heart, which weighed 590 grams, with very marked dilatation of all cardiac chambers, (3) marked dilatation of the aortic valve, with insufficiency, (4) edema of all pulmonary lobes, (5) partial occlusion of both coronary ostia by the dissecting aneurysm, (6) passive congestion of the liver and spleen, (7) ascites, and (8) moderate bilateral hydrothorax and hydropericardium. There was no evidence of inflammation; the media of the aorta showed only marked fibrosis.

#### COMMENT

Previous to 1933, the diagnosis of dissecting aneurysm of the aorta had been made during life in only seven cases. Since that time the ante-mortem diagnosis has been made in 25 additional instances, bringing the total to 32 (7.9 per cent) out of 431 reported dissections. In the cases in which a diagnosis was made during life there were certain suggestive manifestations that pointed to the lesion. Among these were (1) a sudden onset of severe tearing or crushing pain, usually thoracic, reaching its maximum intensity at once in a person with a history of hypertension; (2) wide but variable radiation of pain to the neck, head, back, abdomen, or lower extremities, or to all of these, but rarely to the arms; (3) moderate to extreme collapse, even though the blood pressure was maintained for some time at a high level; (4) a rapid, enlarged heart; (5) a rapid change in the roentgenologic appearance of the aortic shadow; and (6) patchy and bizarre neurologic changes in the legs.

Dissecting aneurysm of the aorta is often confused with coronary thrombosis,<sup>21, 22</sup> and is considered first in the differential diagnosis.<sup>23</sup> It must be remembered that the dissection may invade the root of the aorta, as well as the first portion of a coronary artery; the resulting ischemia may produce acute myocardial infarction, with typical electrocardiographic changes.<sup>24</sup> Extravasation of blood may also occur, and the resultant electrocardiographic changes are characteristic of coronary occlusion.<sup>25</sup> Syncope has already been emphasized as an important clinical feature at the onset of the dissection,<sup>26, 27</sup> and as an aid in the differential diagnosis from coronary thrombosis.<sup>25</sup>

Maintenance of hypertension through the course of the illness, or for some time at a high level,<sup>27</sup> has been considered an important feature, but Hamburger and Ferris<sup>25</sup> recorded this in only one of their six recent

cases. Gouley and Anderson<sup>28</sup> noted particularly the associated aortic murmurs of chronic dissections which simulate those of syphilitic cardiovascular disease. The cardiac hypertrophy may increase very rapidly after the dissection.<sup>27, 28</sup> The ieterus index may be elevated as long as two weeks after the onset of the dissection.<sup>30</sup>

As with aortic insufficiency, the earliest tendency was to attribute the lesion to strain on the heart or even direct trauma; the latter was quite common, but with recognition and acceptance of the fact that syphilis may cause such a lesion, the opinions swung to the other extreme.<sup>31</sup> A middle course is now followed, as syphilis is generally absent in the majority of cases.<sup>32</sup> However, even in the presence of a syphilitic aneurysm of the aorta, acute dissection can occur independently.<sup>24</sup> In the old, "silent" cases, the dissecting aneurysm may readily be confused with one of syphilitic origin.<sup>20, 28, 33</sup> Patchy and bizarre neurologic changes in the legs which occur as the result of circulatory deficiencies in the spinal cord caused by rupture of the intercostal and lumbar arteries are of great importance.<sup>34, 35</sup>

"Healed" or "arrested" dissecting aneurysms may allow the patient to survive for months or even years. The patient is not out of danger even when he has survived the dissection, for the "healed" channel is still prone to complete rupture as a result of imperfections in its walls.<sup>36</sup> One of Rogers' patients lived 27 months after the acute attack,<sup>34</sup> and Roberts<sup>37</sup> was of the opinion that the aneurysm in one of his cases had formed about three years before death. East<sup>38</sup> followed his patient, a 43-year-old white woman, from the first typical symptoms of dissecting aneurysm to her sudden death from rupture of the newly formed sac five years later.

Weiss, Kinney, and Maher<sup>39</sup> reported three cases that were unusual, not only because the dissecting aneurysm was completely "healed," but also because atherosclerosis was present in the new channel in the wall of the aneurysm. The biggest dissecting aneurysm on record, which occurred in a 15-year-old white male with a negative past history, was described in 1939;<sup>40</sup> the dissection affected the whole aorta and its main branches, and the process extended into the lower limbs as far as the popliteal artery on the left and the posterior tibial in the lower third of the leg on the right. There was also dissection of the pulmonary artery and its main branch; this had not been previously described. Only one case of coarctation of the aorta with a terminal dissecting aneurysm<sup>41</sup> has been reported since 1933, which brings the total of such cases to 14. In the period covered at the Cook County Hospital, namely, from 1929 to 1941, there was one patient with coarctation of the aorta with rupture who came to autopsy, but no dissecting aneurysm was present.

#### SUMMARY

The clinical aspects and the post-mortem observations in 19 cases of dissecting aneurysm of the aorta are described. Clinically, these pa-

tients presented (1) old dissections, with intractable heart failure, which had (a) a "silent" history and course in regard to the dissection, or (b) an active history and course, with repeated attacks of severe pain in the chest that radiated into the neck and back; and (2) recent dissections with (a) a typical onset of pain or collapse and (b) an atypical onset with severe dyspnea.

Physical signs of a variable character, such as cardiac murmurs, were outstanding, and did not conform to any definite pattern. The majority of patients with dissecting aneurysm of the aorta do not have a typical onset or course; the latter may extend over many months, but at some time present any or all of the physical signs which have been discussed.

NOTE: Since this article was submitted for publication, two excellent discussions on the subject have appeared:

Sailor, S.: Dissecting Aneurysm of the Aorta, *Arch. Path.* 33: 704, 1942.

Mote, C. D., and Carr, J. L.: Dissecting Aneurysm of the Aorta, *AM. HEART J.* 24: 69, 1942.

Each article represents a different aspect, the former on the pathology, and the latter on the medicolegal viewpoint.

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## ELECTROCARDIOGRAPHIC CHANGES FOLLOWING ELECTRICALLY INDUCED CONVULSIONS

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SINCE the publication of our report dealing with the electrocardiographic changes following metrazol-induced convulsions,<sup>1</sup> a new type of convulsant<sup>2</sup> has been introduced for the treatment of certain psychoses. In this method a convulsion is produced by passing a high frequency alternating current between electrodes placed on either temple.\* We refer to this technique as electro-coma therapy.

Certain advantages of this method, such as ease of administration, more uniform reaction, and less violent convulsions, suggest that this form of treatment will largely replace metrazol. For this reason it seemed worth while to repeat our observations before and after electrically induced convulsions, and to compare them with those which occurred when metrazol was used as the convulsant agent.

Forty-two patients from the private psychiatric practice of one of us (J. L. F.) were selected for this study. All were suffering from major psychoses; depressions were the most common because of their favorable response to this form of therapy. The ages ranged from 19 to 71; the distribution by decades is shown in Table I.

Electrocardiographic observations were made on each patient before and after a major convulsive seizure (lasting from 30 to 50 seconds). The three standard leads of the electrocardiogram were taken just preceding the application of the current, and Lead II was again recorded immediately upon cessation of the convulsion, and at three, five, and ten minutes after the electric shock. Later in our study, a single apex lead was employed in addition to those mentioned above.

### CHANGES IN BLOOD PRESSURE

Blood pressure measurements were made coincidentally with the electrocardiograms whenever the patient's cooperation would permit. In all but one instance there was a rise in the systolic pressure, and this was usually accompanied by a smaller increase in the diastolic. The mean increases were 30 mm. Hg for the systolic, and 9 mm. Hg for the diastolic.

### CHANGES IN HEART RATE

An acceleration in cardiac rate was encountered in nearly all instances. If an arbitrary figure of twenty-five cycles per minute is

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\*The instrument employed in this work was manufactured by Offner Electronics Corporation, Chicago, Illinois. In this machine the "dosage" may be varied by a change in the intensity of the current and the duration of its action. The maximum milliamperage is 700, and the time range from 0.05 to 1.0 second. In all cases the minimum convulsant "dose" is ascertained by starting below the ordinary convulsant level and gradually increasing either the time or intensity. This minimum "dose" is continued or increased slightly throughout the course of treatments.

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TABLE I  
AGE DISTRIBUTION IN DECADES

Age in years	10-19	20-29	30-39	40-49	50-59	60-69	70-79
Number of cases	2	5	12	11	6	5	1

TABLE II  
CHANGES IN BLOOD PRESSURE

CASE NO.	CONTROL	IMMEDIATELY AFTER CONVULSION	3 MIN. AFTER SHOCK	5 MIN. AFTER SHOCK	10 MIN. AFTER SHOCK
1.	105/75	140/75	105/60		100/70
2.	120/80	150/90			
3.	150/80	210/90		140/70	145/75
4.	120/80	160/80			
5.		120/70	145/95	120/65	
6.	150/95	185/100	155/85		145/80
7.	125/100	150/105			
8.	130/90	155/95	135/95		125/90
9.	165/105	215/110	210/100	180/100	180/110
10.	120/80	140/85	130/80		110/80
11.	120/80	130/90			135/90
12.	120/80	140/75		125/75	120/70
13.	125/80	140/85	140/85		125/60
14.	130/80	135/80	135/85	130/80	
15.	145/80	210/100		170/80	
16.	135/90	145/75		140/80	130/70
17.	140/80	140/90	145/75	130/70	135/60
18.	115/70	120/75	135/70		120/75
19.	135/80	150/90	145/95	140/90	140/90
20.	130/75	170/90		150/85	
21.	120/75	140/90		140/70	
22.	160/85	180/90	160/90		130/70
23.	140/80	160/90		150/90	150/80
24.	135/80	165/80	160/90		145/75
25.	140/75	160/90		150/95	140/80
26.	110/60	135/70		130/75	125/75
27.	115/70	150/80		130/80	120/70
28.	110/50	140/90	160/80	135/70	110/60
29.	130/80		160/90	160/90	110/70
30.	120/80	150/90	135/60		110/70
31.	115/60	170/90		140/80	135/75
32.	130/70	180/70		140/70	130/60
33.	140/90	180/100	190/110		130/80
34.	130/80	170/90	150/80	140/75	115/70
35.	120/70	160/80	130/70		110/65
36.	110/70	140/60		110/60	
37.	110/80	130/70		130/50	
38.	160/90	180/80		130/70	120/80
39.	160/100	180/?		150/100	155/100
40.	155/80	240/120	190/90	175/90	190/80
41.	135/85	170/100	180/80	150/80	150/85
42.	120/80	125/80	130/80	125/70	80/50

assumed to constitute a significant change, there were only ten cases in which the rate was not increased by this amount, and in only one was there a decrease. This is in contrast with the rates after metrazol therapy, when no consistent change occurred. Furthermore, there were none of the extremely slow rates; the single bradycardia was of nodal origin, with a rate of 58 per minute.

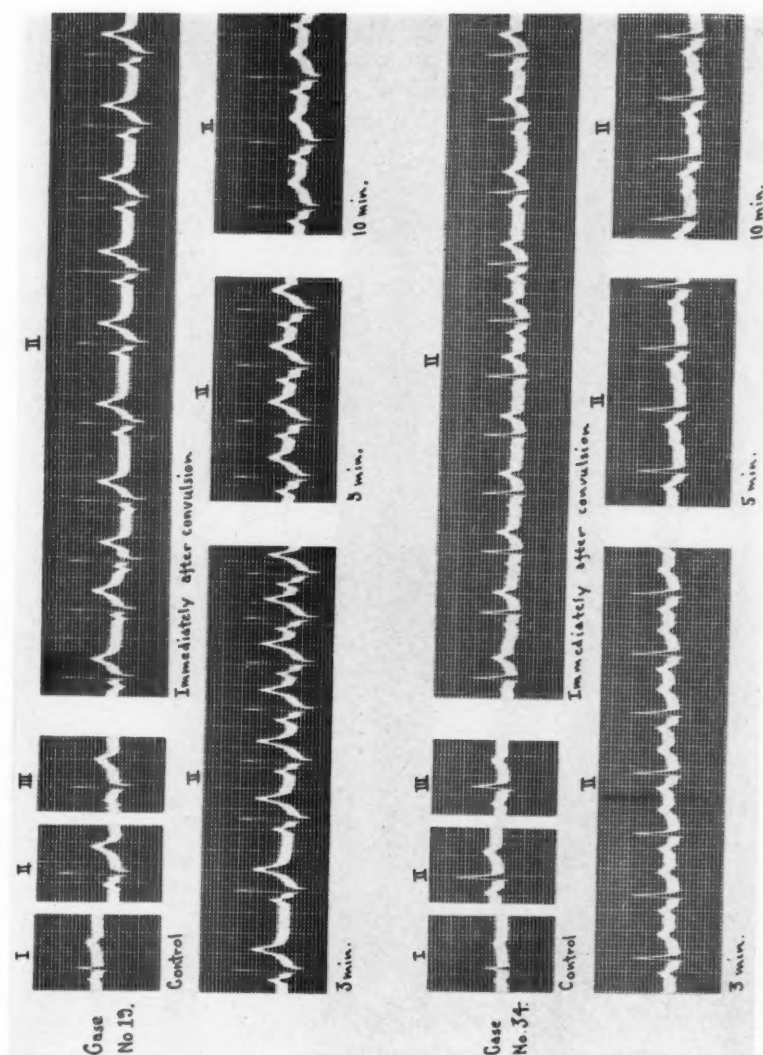


Fig. 1.—Case 19. Nodal rhythm immediately after the convulsion. Note the change in the amplitude and contour of the T wave.  
Case 34. Shifting pacemaker immediately after the convulsion.

#### CHANGES IN RHYTHM

Contrary to the situation after metrazol convulsions, cardiac arrhythmias were not conspicuous. Although there was some change in cardiac rhythm (Fig. 1) in fifteen of the cases, in only two instances was the arrhythmia of a gross nature. These changes were usually present in the record taken immediately after the convulsion, and in all instances the rhythm had returned to normal in the 5-minute record. It can be seen from Table III that the arrhythmias were of two types: those produced by changes in the heart rate and location of the pacemaker; and those resulting from extrasystoles of various types.

TABLE III  
TYPE AND FREQUENCY OF ARRHYTHMIAS

TYPE	NO.
Sinus arrhythmia (marked)	2
Shifting pacemaker	4
Atrioventricular rhythm	3
Auricular extrasystoles	7
Atrioventricular extrasystoles	1
Ventricular extrasystoles	2
Number of convulsions after which the above observations were made	15
Number of convulsions after which no significant arrhythmia was observed	26

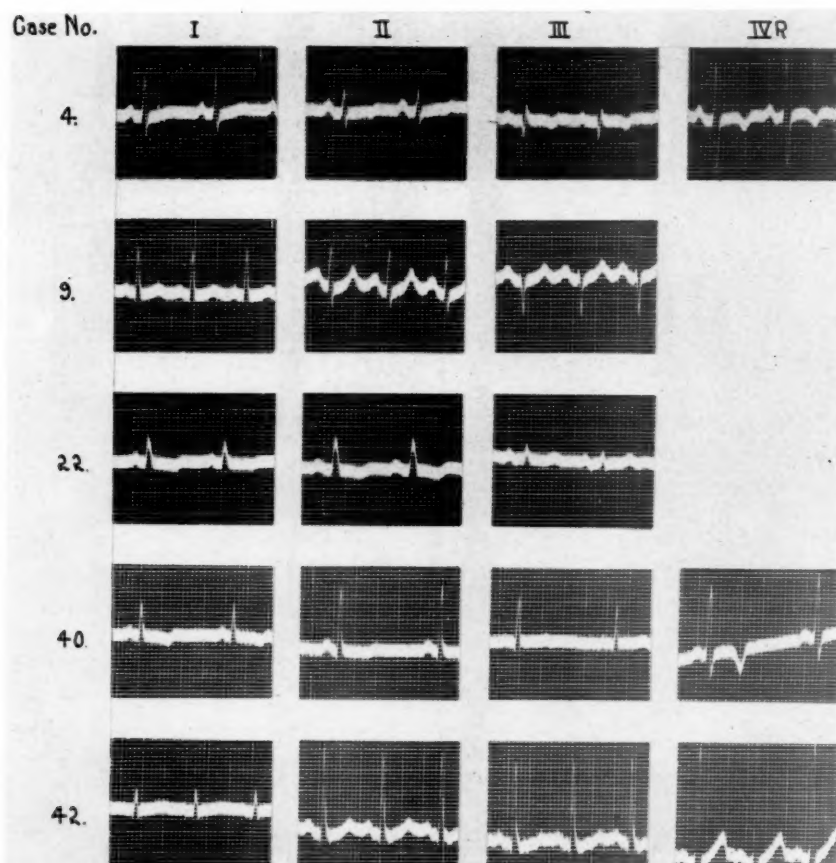


Fig. 2.—Electrocardiograms in the cases in which the cardiovascular system was abnormal.

We cannot say definitely from these observations what mechanism is responsible for the alterations in rhythm. It seems probable that the changes in the location of the pacemaker were the result of vagal stimulation induced by the sharp rise in blood pressure which occurred in most instances.

## CHANGES IN THE T WAVE

An increase in the amplitude of the T wave was encountered in all but eight of the cases. This increase in height was accompanied by a change in contour; the wave became more pointed, and narrow at the base. These resembled the T waves after metrazol-induced convulsions. Since these changes are similar to those which occur in acidosis,<sup>3</sup> the possibility exists (as in the case of metrazol) that there is a temporary acidosis immediately after the convulsion. This might be produced by the extreme muscular activity during a period when respiration is diminished or absent. Contrary to the observations of Bellet<sup>4</sup> and his associates, we had no instances in which the T wave became inverted, or the S-T segment significantly elevated, after treatment.

## CASES IN WHICH THE CARDIOVASCULAR SYSTEM WAS ABNORMAL

There were five cases in this series in which the cardiovascular system was abnormal. In three cases, Nos. 9, 22, and 40, the patients had hypertension, and their electrocardiograms are shown in Fig. 2. Case 4 was that of a fifty-five-year-old woman who had had angina pectoris for many years, in whom Dr. Claude Beck had established a collateral coronary bed by operation on July 30, 1937. In each of these patients the critical nature of the mental condition was such that the risk of treatment seemed justified. All were given the usual course of seizures without complication, and the electrocardiograms after treatment did not differ from those of other patients in this series. In this group we were particularly interested in knowing whether the convulsion might not be followed by a period of myocardial anoxemia. Our attention was, therefore, directed to the S-T segment in the standard and apex leads, but in no instance were these significantly altered.

Case 42 was that of a fifty-eight-year-old man with chronic valvular disease of rheumatic origin. He had mitral stenosis and insufficiency and moderate cardiac enlargement, but there were no signs of cardiac failure. This patient's mental illness was extremely severe. He refused all food, and, in spite of forced feedings, he lost seven pounds in weight during his first week in the hospital. Twenty minutes after the patient's first convulsion he perspired profusely, and became pale, cold, and clammy. The blood pressure, which, during the treatment, had been in the neighborhood of 125/80, fell at this time to 70/30. He was given 0.5 Gm. of caffeine citrate and two 0.3 c.c. doses of adrenalin hydrochloride (1:1,000 dilution). In another twenty minutes the blood pressure had returned to its former level and he appeared normal again. The electrocardiogram at this time was identical with the control record, taken before the seizure had begun. This reaction was different from anything we had seen before, and cannot be satisfactorily explained. Whether the peripheral vascular collapse was associated in some manner

with the cardiac lesion cannot be stated with certainty, but it seems rather unlikely. No late untoward results have developed, but treatment was not resumed.

#### CONCLUSIONS

The electrically induced convulsion was followed by a rise in both the systolic and diastolic blood pressure, an increase in heart rate, and certain transitory electrocardiographic changes. The T waves of the electrocardiogram were increased in amplitude, and, in some cases, a change in rhythm was observed. These alterations in the cardiovascular system were less marked than those which occurred after metrazol-induced convulsions.

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## STUDIES ON CORONARY OCCLUSION

### III. THE EFFECT OF DIGITALIS ON THE RS-T SEGMENT OF THE ELECTROCARDIOGRAM AFTER CORONARY LIGATION

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DIGITALIS should not be used in coronary artery disease unless there is heart failure which has not responded to any other treatment.<sup>1-8</sup> There are three principal reasons for this. First, digitalis increases myocardial irritability; consequently, a dangerous or fatal ectopic rhythm may result from a further increase of myocardial irritability in a heart which already has an abnormally irritable focus in the areas of infarction. Secondly, digitalis increases the strength of the cardiac contraction; this would increase the danger of dislodging mural thrombi after occlusion. Furthermore, the resultant rise in intraventricular pressure may cause aneurysmal dilatation of the infarcted ventricle, or may increase any already existing dilatation. Thirdly, digitalis is believed to cause constriction of the coronary arteries. The constriction may occur both directly, by the smooth muscle action of digitalis, and indirectly, through nervous impulses mediated by way of the centrally stimulated vagus.

The question whether digitalis actually does produce coronary artery constriction has been extensively investigated, both experimentally and clinically. Suggestive of coronary spasm are the attacks of thoracic oppression after overdosage with digitalis in patients treated for cardiac failure.<sup>3</sup> In animal experiments, Meyer<sup>9</sup> and Sakai and Saneyoshi<sup>10</sup> found that digitalis did not constrict the coronary vessels *in situ*. As a result of these studies, Eggleston<sup>11</sup> advanced the now prevalent opinion that digitalis is not contraindicated in cases of cardiac failure complicated by angina. Gold, et al.,<sup>12</sup> found that digitalis did not differ from placebos in its effect on cardiac pain. From this they concluded that "... digitalis even in large doses rarely, if ever, produced effective constriction of the coronary arteries in man." Bond<sup>13</sup> measured coronary vein outflow in dogs, and found that digitalis was without effect. Using a Starling heart-lung preparation and a Morawitz cannula, Bodo<sup>14</sup> observed increased flow after digitalis, and concluded that digitalis actually dilated the coronary vessels. Fenn and Gilbert<sup>15</sup> found that, in dogs, digitalis caused a decrease in coronary sinus outflow. The effect did not appear after section of the vagi. Voegtlin and Macht<sup>16</sup> observed contraction of isolated rings of ox and pig coronary arteries in response to certain digitalis bodies, but relaxation after certain others.

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They recommended the administration of nitrites along with digitalis in those cases in which coronary constriction must be avoided. Ginsberg, Stoland, and Siler<sup>17</sup> used various commercial digitalis preparations on intact dogs and in heart-lung preparations (Morawitz cannula). Their results were inconsistent, more so in the intact animal than in the heart-lung preparation. They formed the opinion that coronary constriction, if it occurs after digitalis administration, is not of sufficient degree to constitute a contraindication to the drug in any but cases of severe coronary insufficiency. Essex and his associates,<sup>18, 19</sup> using the thermostromuhr, observed no change in the coronary blood flow in dogs as a result of administering the digitalis glycosides. Haskell, et al.,<sup>20</sup> found that, as compared to cats, dogs were poor subjects to use in digitalis studies because of their inconsistent reaction to this drug. Therefore, results obtained with digitalis on the dog must be interpreted with caution. Routier and Puddu<sup>21</sup> stated that the changes in the T wave which they observed were not due to an effect of digitalis upon the coronary vessels because, in cases of coronary artery disease, digitalis did not exaggerate the electrocardiographic changes produced by effort. In 1941, Liebow and Feil<sup>22</sup> stated that "the effect of this drug [digitalis] on the coronary arteries is still not known."

From this confusing mass of clinical and experimental material and opinion, it is impossible to arrive at any satisfactory conclusion concerning the effects of digitalis on the coronary arteries. It is the purpose of the data herein presented to cast further light on this problem from a somewhat different experimental approach.

The authors<sup>23, 24</sup> demonstrated that, after coronary ligation in cats, the induction of generalized anoxemia increased the RS-T segment deviation of the electrocardiogram, probably because the induced anoxemia increased the local myocardial anoxia caused by the ligation. Levy and his co-workers<sup>25</sup> obtained similar reactions in cases of human coronary insufficiency, and accorded diagnostic value to the changes in the T wave which occur during induced anoxemia. The only consistent results obtained by us were changes in the RS-T segment deviation. The reaction to induced anoxemia suggested a new approach to the problem of how digitalis affects the coronary circulation. *If, after coronary artery ligation, a drug increases the deviation of the RS-T segment of the electrocardiogram, or if the drug causes its reappearance after recovery, it may be concluded that the drug had caused an increase in the local myocardial anoxia, presumably by vasoconstriction.* The following experiments were designed to ascertain the effects of digitalis upon the RS-T segment deviation after coronary ligation, before and during induced anoxemia.

#### METHOD

Sixty-three male or nonpregnant female cats, weighing at least 2.5 kg. each, were used in two series of experiments. In Series A, comprising seventeen cats,

the left branch of the left anterior descending coronary artery was ligated according to the technique already described.<sup>24</sup> On each of nine cats observations were made one week before operation, immediately after operation, and weekly for two or three weeks after operation. On eight cats observations were made only immediately after operation. All observations were made with the animals under light sodium pentobarbital anesthesia (30 mg. per kilogram, intraperitoneally), which has been shown to have no influence on the level of the RS-T segment of the electrocardiogram.<sup>23</sup> Standard three-lead electrocardiograms were made on each animal before and during the fifteen-minute administration of an atmosphere of 10 per cent oxygen. After the period of anoxemia, at least fifteen minutes of air breathing were allowed, and then crystalline ouabain\* (0.25 mg. per cubic centimeter) was injected intramuscularly (0.1 mg. per kilogram). Thirty and forty-five minutes after the ouabain, electrocardiograms were made. One week after operation, electrocardiograms were made on seven of the first nine cats after the intramuscular administration of pitressin (1 unit per kilogram).

In Series B there were forty-six cats. Twenty-three were subjected to coronary ligation, and ten were controls which were not operated on. Twenty minutes after the coronary ligation, a continuous intravenous infusion of ouabain in saline at the rate of 1 c.c. per minute was started. The dilution of the ouabain was so adjusted for each cat that 3.3 micrograms per kilogram were administered per minute (0.1 mg. per kilogram would thus be administered in thirty minutes). The moment of cardiac standstill was recorded as the end point of this experiment.

Travell, et al.,<sup>26</sup> stated that in the cat with partially healed cardiac infarction (three weeks after operation), the fatal dose of digitalis is about 25 per cent less than for the normal cat, or for a cat immediately after operation. Because of this statement we subjected thirteen cats to coronary ligation, but did not give the ouabain solution until a week after the ligation. Each of the last five of these cats was infused simultaneously with two other cats; one was a control which had not been operated upon, and another had just been operated upon. Each of these five groups of three cats thus formed a unit, each member of which served as a control for the others.

## RESULTS

### *Series A—Seventeen cats.—*

1. Preligation electrocardiographic studies were done on nine cats. During the anoxemia two of these developed deviation of the RS-T segment. The average (sum of the deviations in 3 leads) for the nine cats was 0.2 mm. Complete return to the original state occurred when the cats were allowed to breathe air. The intramuscular administration of ouabain caused an RS-T segment deviation which averaged 0.4 mm. in six of the nine cats. After ouabain, anoxemia decreased the RS-T segment deviation in two of the six cats; the average was now only 0.3 mm.

Coronary ligation was deferred until one week after these control studies to allow sufficient time for elimination of the ouabain. Immediately after the operation eight of the cats showed RS-T segment deviation; the average for the nine cats was 3.2 mm. Anoxemia increased the RS-T segment deviation to an average of 4.0 mm., and all nine cats now showed changes. Upon recovery from the anoxemia and after the intramuscular administration of ouabain, the average RS-T segment de-

\*Ouabain, Arnaud.

viation in eight cats was 4.3 mm. In the ninth cat there appeared a continuous run of ventricular premature beats, so that the RS-T deviation could not be studied. While under the influence of ouabain and during anoxemia, six of the cats showed an average RS-T segment deviation of 5.3 mm. One of the other cats developed right bundle branch block, with premature beats. A second showed a reversal of the direction of the RS-T segment deviation in all 3 leads, from a total elevation of 5.0 mm. to a depression of 2.5 mm.

In an effort to ascertain whether any of the observed ouabain effects were caused by central vagus action, atropine was given intravenously. There resulted an insignificant decrease in the total RS-T deviation.

The entire procedure, as described above, was repeated on the six surviving cats two or three weeks after the ligation and one or two weeks after pitressin, as described below. All six cats showed RS-T segment deviation which averaged 1.8 mm. During anoxemia this rose to an average of 2.2 mm.; three cats showed an increase and two a decrease. After the intramuscular administration of ouabain, all six cats showed increased RS-T segment deviation, which now averaged 3.4 mm. Anoxemia reduced the average deviation slightly (to 3.3 mm.); three cats showed a decrease, one an increase, and two no change.

*The Effects of Pitressin:* One week after the ligation, the RS-T segment deviation averaged 2.5 mm. in seven of the nine surviving cats; one of the seven showed no deviation. During induced anoxemia the average was 2.9 mm. Upon recovery from the anoxemia, pitressin (1 unit per kilogram) was injected intramuscularly. The pitressin increased the average RS-T segment deviation to 4.0 mm., and all seven cats were affected. During the course of the pitressin action, induced anoxemia resulted in a fall in the average RS-T deviation to 2.8 mm. in six cats; the seventh died after developing ventricular extrasystoles.

2. In the 8 cats upon which no preoperative observations had been made, there was an initial, average, postligation RS-T segment deviation of 1.5 mm. During anoxemia, the deviation increased to 1.8 mm. After the intramuscular administration of ouabain the deviation averaged 1.0 mm. in seven cats; the eighth developed a continuous run of extrasystoles. During the period of ouabain activity anoxemia increased the average RS-T segment deviation to 2.5 mm. in the seven cats; the aforementioned eighth cat continued to have the extrasystoles.

These results of the studies of the complete Group A are represented graphically in Fig. 1.

*Series B—Forty-six cats.—*

In this experiment the animals were subjected to a continuous infusion of ouabain in saline until cardiac standstill occurred. In twenty-three of the animals the infusion was started immediately after coronary artery ligation. In thirteen cats infusion was withheld until a week after the

ligation. The ten control animals were not subjected to coronary artery ligation, although pericardiotomy had been carried out in some.

The above experiments were performed in two groups. The initial group contained thirty-one cats. The animals with ligated coronary arteries died sooner after the start of the infusion than did the controls. There seemed to be little difference between the cats which were infused immediately after the operation and those which were infused one week after operation. In order to minimize the accidental distribution of these results, it was decided to run an additional series of fifteen cats in five parallel groups of three animals each: one, a control; one cat immediately after the ligation; and one cat which had been operated upon one week earlier. The results in this group agreed with those in the first group, so that the two groups are combined in a single report.

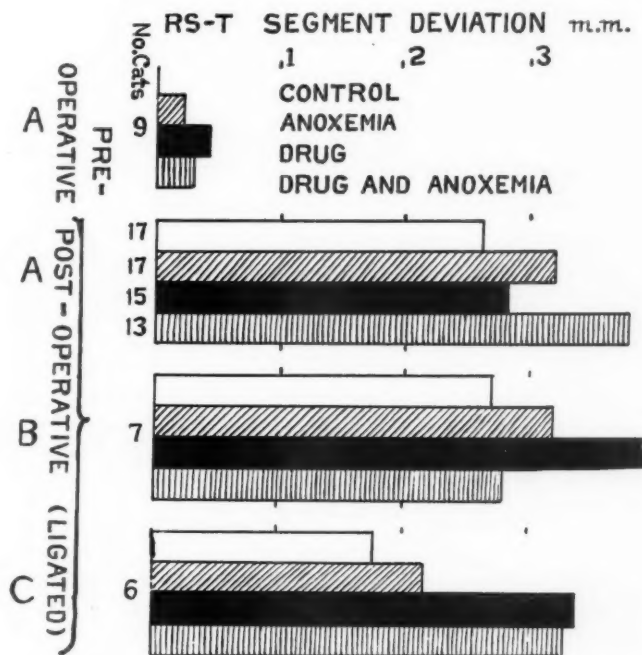


Fig. 1.—The effect of ouabain and pitressin on the RS-T segment of the electrocardiograms of cats (average), before and during induced anoxemia after experimental ligation.

A. Ouabain was given before and immediately after the ligation.

B. Pitressin was given one week after the ligation and the first dose of ouabain.

C. Ouabain was given two to three weeks after the pitressin injections at B.

In the ten control animals death occurred at an average of 60 minutes (35 to 72) after the start of the infusion. In the twenty-three cats which were infused immediately after the ligation, death occurred at an average of 50 minutes (37 to 62) after the start of the infusion, and in the thirteen cats which were infused one week after operation, death occurred at an average of 55 minutes (30 to 75) after the start

of the infusion. Thus, the ligation resulted in an increase of 16.7 per cent in sensitivity to ouabain in the cats which were studied immediately after operation, and in an increase of but 8.3 per cent when they were tested a week after operation. The scatter of the values for each group is such as to render insignificant the differences in the average of the three groups of cats. The over-all average of the forty-six cats was 53.6 minutes.

#### DISCUSSION

In the first group of experiments ouabain caused an increase in the deviation of the RS-T segment of the electrocardiogram after coronary artery ligation, although it did not do so in the normal cat. Similar results were obtained when pitressin was used one week after coronary ligation. It is reasonable to infer that the increase in the RS-T segment deviation from both ouabain and pitressin was due to the same cause, i.e., an increase in the myocardial anoxia produced by coronary artery constriction.

The RS-T segment deviation caused by the ligation was increased by the institution of anoxemia, which confirms our previous observations.<sup>24</sup> It corroborates the thesis that the RS-T segment deviation which follows ligation is a reflection of local myocardial anoxia, and can be exaggerated by induced anoxemia or by vasoconstrictors, such as pitressin. Since ouabain increased the RS-T segment deviation after ligation, and since this increase was further augmented by induced anoxemia, we have come to the conclusion that, after coronary ligation, ouabain causes coronary vasoconstriction.

Contrary to expectation, anoxemia resulted in a diminution of the large RS-T segment deviation which followed the administration of pitressin. It is assumed that the electrocardiographic changes which occur after the ligation of a coronary artery result from impaired oxygenation of that part of the myocardium normally supplied by the ligated vessel. The degree of local myocardial anoxia may be increased by the administration of a coronary constrictor, such as pitressin, or by the induction of generalized anoxemia by the administration of an atmosphere of 10 per cent oxygen. However, during generalized anoxemia of the type induced in these experiments, there are a rise in blood pressure of central origin, and an increase in the heart rate which is mediated through the sympathetic division of the autonomic nervous system.<sup>27</sup> The sympathetic supply to the coronaries is vasodilator, so that, other things being equal, anoxemia would increase the blood flow through the coronary arteries. The induction of anoxemia after pitressin may actually bring about an increase in flow through the coronary vessels, both by raising the blood pressure and by reflexly diminishing coronary arterial tonus, thus relieving somewhat the local myocardial anoxia. It is not suggested that the induction of anoxemia is necessarily a beneficial procedure, for the apparent electrocardio-

graphic improvement occurred only after severe embarrassment of the central nervous system by the anoxemia. Actually, the RS-T segment deviation in the cats with ligated arteries is more elevated by pitressin and anoxemia than by anoxemia alone.

Liebow and Feil<sup>22</sup> studied the electrocardiograms of digitalized patients during exercise. They concluded that the electrocardiographic changes which they observed during exercise resulted from a diminished oxygen supply to the heart. In this case it is probable that the vasoconstrictor effects of digitalis exaggerated the myocardial anoxia of exercise, giving results which are similar to those obtained by us in cats.

Study of our second group of animals showed that cats which are treated immediately after coronary ligation are 17 per cent more sensitive to the lethal effects of ouabain than similarly treated controls which were either unoperated upon or had been subjected to pericardiotomy without ligation. Travell, et al.,<sup>26</sup> found no difference in susceptibility in their animals. These authors also found that cats were more susceptible to the digitalis bodies three weeks after coronary ligation than immediately after ligation. In our experiments, no great difference was observed between the two groups of animals. In fact, the cats which were infused with ouabain one week after ligation withstood larger doses of ouabain than those which were infused immediately after operation. The difference in the minimal lethal dose of ouabain between the controls and the cats with ligated arteries was not sufficiently great to warrant the conclusion that digitalis therapy is contraindicated after coronary occlusion in man.

#### SUMMARY

1. Ouabain was administered to seventeen cats before, immediately after, and two to three weeks after, coronary ligation.
2. The ouabain further increased the RS-T segment deviation which was induced by the ligation.
3. Pitressin, administered one week after coronary ligation, resulted in an exaggeration of the RS-T segment deviation.
4. Anoxemia, induced after coronary ligation, increased the RS-T segment deviation resulting from the ouabain, but decreased that produced by pitressin.
5. The minimal lethal dose of ouabain was less in cats with experimental coronary occlusion than in the controls, but increased somewhat when a week was allowed to elapse after the operation.
6. From the experiments detailed above, it is concluded that the digitalis bodies cause constriction of the coronary arteries of the cat. However, the constriction is not sufficiently great to increase significantly the toxicity of ouabain in cats with ligated arteries.
7. Our results do not indicate that digitalis is an especially dangerous drug to use after coronary occlusion in man.

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## STUDIES ON CORONARY OCCLUSION

### IV. VASODILATORS AND THE CORONARY CIRCULATION EXPERIMENTAL OBSERVATIONS

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IN THE preceding paper<sup>1</sup> we reported that, after coronary artery ligation in the cat, digitalis and pitressin increased the RS-T segment deviation of the electrocardiogram both before and during induced anoxemia. This was interpreted to indicate that digitalis, like pitressin, constricted the coronary arteries. As a consequence of these observations, the effect of several so-called coronary dilators was investigated, using as the criterion of action the changes in the RS-T segment before and during anoxemia. These criteria are similar to those employed clinically,<sup>2</sup> and show promise of being useful as an approach to the problem of the pharmacodynamics of the impaired coronary circulation.

In cases of human coronary insufficiency, Levy and his collaborators,<sup>3</sup> using the electrocardiographic effect of induced anoxemia as an index of coronary blood flow, reported that various drugs increased coronary circulation. Other investigators,<sup>4-11</sup> who employed a variety of methods of observation in animals, reported conflicting results from the use of the "coronary dilators." Coronary perfusion experiments and experiments on isolated segments of coronary arteries yield results which are not comparable directly to those which are obtained on intact animals.

The heart with an experimentally induced infarct may be considered as benefited by a given drug if the average size of the infarct is less than in untreated animals. This did not prove to be the case in a series of cats treated with papaverine,<sup>12</sup> and in another series reported by Gold, et al.,<sup>13</sup> who used aminophylline. In both series the cardiac infarcts of the treated animals were of greater average size than those of the untreated controls. Fowler, Hurevitz, and Smith<sup>6</sup> performed similar experiments on dogs, and found that the infarcts of the dogs treated with aminophylline were smaller than those of the untreated controls. It is suggested that these results were fortuitous, and that no conclusion should be drawn from data obtained by this method.

The present report deals with experiments which we believe to be less open to objection than those recounted above. By means of induced anoxemia after experimental cardiac infarction, a study was made of the effect of nitroglycerine, papaverine hydrochloride, and aminophylline upon the RS-T segment deviation of the electrocardiogram. The efficacy of the drugs was to be judged by the amount by which they reduced the

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RS-T segment deviation caused by coronary ligation, under usual conditions as well as during induced anoxemia.

#### METHOD

Under sodium pentobarbital anesthesia the left branch of the left anterior descending artery was ligated in each of 16 cats, according to the technique previously described.<sup>14a, 14b</sup> The cats were males or females, and weighed at least 2.5 kilograms each. The influence of each of the three drugs was observed immediately after the operation and at weekly or biweekly intervals thereafter. All observations were made with the animals under light pentobarbital anesthesia (30 mg. per kilogram), which has been shown to have no influence on the RS-T segment.<sup>12</sup> A fifteen-minute period of anoxemia (10 per cent oxygen) was followed by a recovery period of at least fifteen minutes of air breathing. The drugs were administered intraperitoneally because of the ease of injection; in order to reduce to a minimum any effects on blood pressure (discussed later), such as might occur after an intravenous injection of vasodilators; and in order to obtain more prolonged drug action than is usual after intravenous administration.

Electrocardiograms were made before and ten minutes after the administration of nitroglycerine, and again near the end of fifteen minutes of anoxemia. Another fifteen-minute recovery period brought the time to forty minutes after the administration of the nitroglycerine; this period was deemed ample for the full development of the action of the drug. Papaverine hydrochloride was then injected. In order to ascertain whether there were mixed drug effects, 8 sets of observations were made with papaverine, but without the previous administration of nitroglycerine. The injection of aminophylline was made forty-eight hours later in order to avoid an additive effect with the papaverine.

Forty-three sets of observations were made on the 16 cats. The dosages were varied over a wide range, as indicated in the following schedule.

1. Nitroglycerine—0.1, 0.25, 0.5, 1.0 mg. per kilogram.
2. Papaverine hydrochloride—3.0, 5.0, 10.0 mg. per kilogram.
3. Aminophylline—5.0, 10.0, 15.0 mg. per kilogram.

Blood pressure studies were made in the usual manner.

#### RESULTS

##### 1. *Preoperative Observations* (16 cats).—

a. *Control*.—In 5 cats the total RS-T segment deviation was 3.0 mm. The average deviation for the 16 cats was 0.2 mm. During induced anoxemia the total deviation was 1.5 mm.; changes in the electrocardiograms of 2 cats accounted for the decrease. The average deviation was 0.1 mm.

b. *Nitroglycerine*.—The average RS-T segment deviation was 0.2 mm. During induced anoxemia the average increased to 0.3 mm.

c. *Papaverine Hydrochloride*.—The average RS-T deviation was 0.2 mm., with an increase to 0.3 mm. during anoxemia. Since the papaverine was injected during the period of nitroglycerine action, these figures show no further increase as a result of the papaverine.

d. *Aminophylline*.—The average RS-T segment deviation was 0.2 mm., with a decrease to 0.1 mm. during anoxemia.

It is evident that the administration of these drugs before the ligation caused only minor changes in the RS-T segments of the electrocardiograms of 5 of the 16 cats. These 5 cats might have been discarded as hypersensitive. They were not discarded in order to avoid over-weighting the results in favor of the drugs, and also in order to stress the importance of performing control observations on animals intended for coronary ligation.

## 2. Postoperative Observations.—

Postoperative observations were made at intervals from immediately after, to eighty-five days after, the ligation. Characteristic effects were noted throughout the postoperative period.

a. *Control*.—Ligation caused the appearance of an RS-T segment deviation in 15 of the 16 cats which totalled 67.0 mm. in the 43 observations. The average deviation per observation was 1.6 mm. During induced anoxemia all of the 16 cats showed an RS-T segment deviation which totalled 96.0 mm., and an average deviation of 2.2 mm., or an increase of 37.5 per cent.

b. *Nitroglycerine*.—There were 35 observations. The average deviation was 2.1 mm., or 31 per cent higher than before the drug. After the induction of anoxemia this increased to 2.4 mm.

c. *Papaverine Hydrochloride*.—Forty-three observations were made. The average deviation was 1.9 mm. This deviation is to be compared with 2.1 mm. as a control, for the papaverine was administered after the nitroglycerine. Therefore, papaverine resulted in a 10 per cent depression of the RS-T segment. During anoxemia the deviation was increased to 2.1 mm., or 13 per cent less than in the control. This "beneficial" effect of papaverine is shown also in the 8 observations which were made without the previous administration of nitroglycerine. These observations were made from six to eighty-four days after operation. The control readings, with air, averaged 0.56 mm.; 4 cats showed no deviation. This increased to 1.5 mm. under the influence of anoxemia. After papaverine hydrochloride (3 mg. per kilogram), the average deviation was reduced to 0.5 mm. Anoxemia after papaverine gave an average deviation of 0.75 mm., or 50 per cent less than when anoxemia was induced without papaverine.

d. *Aminophylline*.—There were 42 observations. The average deviation was 1.6 mm., which was raised to 2.1 mm. by the induction of anoxemia. These figures compare well with those of the controls.

It is obvious from these results that nitroglycerine and aminophylline, when given in the doses stated, had an adverse effect, or no effect, upon the RS-T segment deviation of the electrocardiogram after coronary occlusion. Since these drugs are smooth muscle depressants, the opposite result was to be expected; therefore, the effect observed by us is not easy to explain. One possibility, which may apply especially to nitroglycerine, is that these drugs may lower the blood pressure

sufficiently to elicit central vasoconstricting effects, but the experiments detailed below show that none of the three drugs, as given by us, lowered blood pressure sufficiently.

Papaverine alone, or after nitroglycerine, lowered the RS-T response of anoxemia, which suggests that this drug does actually dilate the coronaries under the conditions of this experiment.

*3. The Effect of the Vasodilator Drugs Upon the Blood Pressure of the Cat.—*

Nitroglycerine, papaverine hydrochloride, and aminophylline, when injected intravenously, usually cause a fall in blood pressure. To test out the possibility that the surmised beneficial effect of these drugs on the electrocardiogram might have been masked by a fall in blood pressure, experiments were performed on 3 cats after coronary ligation. The drugs were given intraperitoneally and in conformity with the routine of the previous experiments. Over a fifteen-minute period, anoxemia caused a rise in blood pressure of 5 to 15 mm. Hg. Nitroglycerine (0.75 mg. per kilogram) did not affect the blood pressure. Papaverine hydrochloride (15 mg. per kilogram) and aminophylline (25 mg. per kilogram) caused a fall in the blood pressure of 10 to 15 mm. Hg. Such a fall in blood pressure did not elicit any changes in the RS-T segment.<sup>14</sup> Anoxemia, induced during the slight depression of the blood pressure, caused an increase. It may therefore be concluded that the RS-T segment deviations observed after coronary ligation, and any further alteration by the three drugs, were not contributed to by changes in blood pressure induced by the drugs which we used.

DISCUSSION

The data obtained after experimental coronary ligation indicate that, of the three vasodilators, nitroglycerine increased, papaverine hydrochloride depressed, and aminophylline did not modify appreciably, the RS-T segment deviation of the electrocardiogram. The data also indicate that the "coronary vasodilator" effect of these drugs was not masked by a fall in blood pressure, for it was shown (a) that the fall in blood pressure was slight, and (b) that only a much greater fall in blood pressure modifies the RS-T segment.<sup>14</sup>

The lack of effect of aminophylline on the RS-T segment may be due to several causes. (a) The doses used by us may not have been sufficiently large. (b) In experimental coronary ligation of the type employed in these experiments, there is a chance that the collateral circulation is poor, and therefore the drugs may reach the anoxic vessels in insufficient amounts to be effective. We know that blood does reach the area of cardiac tissue involved in the ligation because induced anoxemia increases the RS-T segment deviation which was produced by the ligation.<sup>14</sup> (c) A species difference may explain the beneficial effects obtained in man by Williams, et al.,<sup>2</sup> who used a number of xanthine

derivatives. (d) In man, the pathology of cardiac infarction after "coronary occlusion" differs materially from that of experimental ligation. The noninfarcted cardiac muscle which is still functioning is not normal. (e) It is believed that in the conscious animal, coronary occlusion is regularly accompanied by vasospasm,<sup>15</sup> whereas, in experimental coronary ligation, as it is usually performed, there may be little or no associated vasospasm because of the surgical anesthesia. In fact, it is possible that, in the cat, there is dilation of the blood vessels collateral to the ligated area as a result of the anoxemia, and it may not be possible to increase further this dilation by the use of vasodilator drugs.

The "beneficial" effects of papaverine are in keeping with our previous observations,<sup>16</sup> as well as of those of Linder and Katz,<sup>17, 18</sup> who obtained obvious coronary vasodilation when the perfusion fluid contained papaverine hydrochloride in a concentration of 1:120 to 1:1190; these concentrations could not be attained in *in vivo* experiments. Our own experiments indicate that no such concentrations are necessary, for vasodilator effects were observed with the use of 3 mg. per kilogram intraperitoneally.

#### SUMMARY

1. Observations were made on the effect of nitroglycerine, papaverine hydrochloride,\* and aminophylline upon the RS-T segments of the electrocardiograms of 16 cats under sodium pentobarbital anesthesia. The cats were studied (a) before and during induced anoxemia, and (b) before and at intervals after coronary ligation.

2. The three vasodilators lowered the blood pressure less than 15 mm. Hg, and only for a short time.

3. Lowering of the blood pressure artificially by acute withdrawal of blood had no effect upon the electrocardiogram until a blood pressure of about 30 mm. Hg was reached, when induced anoxemia resulted in a greater RS-T segment deviation than previously.<sup>14</sup>

4. The RS-T segment deviation produced by coronary artery ligation was increased by nitroglycerine; papaverine hydrochloride decreased it after the nitroglycerine, as well as when no previous medication had been given. Aminophylline had no consistent effect.

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\*The papaverine hydrochloride used in these experiments was generously donated by Eli Lilly & Company.

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## Clinical Reports

### CONGENITAL PULMONARY STENOSIS WITH CLOSED CARDIAC SEPTA

REPORT OF A CASE WITH COMMENTS REGARDING THE CIRCULATION TIME

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#### INTRODUCTION

CONGENITAL stenosis of the pulmonary valve with closed cardiac septa is rare. In Maude Abbott's<sup>1</sup> collected series of 1000 cases of congenital heart disease, pulmonary stenosis with closed auricular and ventricular septa occurred nine times. The present case is reported because of the rarity of the lesion and because of the application of circulation time measurements to the diagnosis.

#### CASE REPORT

The patient, a 15-year-old eighth grade pupil, was seen first in March, 1940. She complained of increasing dyspnea and cyanosis of about one year's duration. She had never been cyanotic or dyspneic before. Careful questioning elicited no other complaints. Her birth was normal and she was not a "blue baby." At the age of five she became ill with fever and joint pains. These symptoms subsided in two or three weeks, but she was kept in bed for a year because her attending physician said she had rheumatic fever which affected her heart. For the next eight years she got along well by observing moderate restrictions in her physical activity because of "leakage of the heart." She was formerly well nourished, but in recent years she had become very thin. The father, mother, and two siblings were living and well.

In October, 1932, the patient visited the Mayo Clinic.\* At that time there was no cyanosis. A systolic murmur and thrill were found in the pulmonic area. The roentgenogram of the chest was negative, and the electrocardiogram showed right axis deviation.

On examination the patient appeared poorly developed and poorly nourished. The lips, cheeks, conjunctivae, and mucous membranes were moderately cyanotic, and the fingers and toes were markedly cyanotic. There was clubbing of the fingers and toes. The extremities were cold. The pulse rate ranged from 96 to 116. The blood pressure could not be measured by the auscultatory method, but, by palpation, the systolic blood pressure was 88 to 93 in both arms. The only other abnormalities were those referable to the heart. The apex impulse was in the fifth intercostal space, 6.7 cm. from the midsternal line. There was a pronounced systolic thrill in the second and third left intercostal spaces. The first sound at the apex was loud, and at times it was split. A loud, low-pitched, blowing systolic murmur was heard

\*We are indebted to Dr. R. J. L. Kennedy, of the Mayo Clinic Staff, for this information.

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over the whole precordium and posteriorly in the left interscapular space. The point of maximum intensity of the murmur was in the second left intercostal space, just to the left of the sternum. The pulmonary second sound was diminished.

Fluoroscopic examination showed a normally active heart of normal size. There was marked prominence of the pulmonary conus as viewed in the anteroposterior and right anterior oblique positions. A roentgenogram confirmed the fact that the pulmonary conus was prominent.

The erythrocyte count was 8,100,000 per cubic millimeter, and the hemoglobin was 19.6 Gm. per 100 c.c. The arm-to-tongue circulation time, measured with 10 per cent calcium levulinate, was 10 seconds. When 20 per cent calcium gluconate was used, the circulation time was 11 seconds. Both readings were considered to be within normal limits.

A diagnosis of congenital stenosis of the pulmonary artery, with interventricular septal defect, was made. Activity within the limit of the patient's ability was recommended.



Fig. 1.—The markedly hypertrophied right ventricle is shown above the left ventricle in this photograph of the heart in tranverse section.

The patient continued in school and remained fairly well until December, 1940, when the dyspnea and cyanosis became more intense. When she was seen March 5, 1941, she had mild grippe. The dyspnea was somewhat greater than formerly, but the other features were unchanged. She made a rapid recovery from the acute infection. On March 10, 1941, the patient experienced two attacks of severe dyspnea and died in the second attack. A few hours before death the pulse rate was 112. There were no rales in the lungs and there was no edema of the extremities.

#### POST-MORTEM EXAMINATION

Only a limited autopsy was permitted. The pericardium was normal. The heart was not weighed, but it appeared to be normal in size. The apex was formed by the right ventricle. The auricles were not dilated or hypertrophied. The average thickness of the right ventricular wall was 28 mm. (Fig. 1). The wall of the left

ventricle averaged 21.5 mm. in thickness. The capacity of the right ventricular cavity was estimated at 10 c.c. The cardiac septa were closed. The cusps of the pulmonary valve were fused into a cone, at the apex of which there was an opening 2 mm. in diameter (Fig. 2). At the anterior commissure there was a slit, 3 mm. in length, which did not connect with the above-mentioned opening. The valve surface about the opening was surrounded by a 3 mm. band of pinkish, moderately friable vegetations. The pulmonary artery appeared slightly decreased in diameter, and its wall was smooth. The aortic valve and the aorta were normal. The mitral valve was thickened and slightly deformed by firm, fibrous nodules. There was no fusion of the cusps. The chordae tendineae were thickened and shortened. There were fresh vegetations on the line of closure of the valve. The tricuspid valve was similarly deformed, but to a less extent; there were a few fresh vegetations at the line of closure. The lungs were crepitant and the sectioned surface was dry.



Fig. 2.—The pulmonary artery is laid open to show the slit-like opening in the pulmonary valve which is surrounded by an areola of vegetations. The prosector's middle finger is in the dilated pulmonary conus.

#### COMMENT

In the presence of pulmonary stenosis with a septal defect there is usually a shunt of venous blood from the right side of the heart into the arterial blood of the left side of the heart. In such cases the circulation time from the arm to the tongue is greatly shortened. The stimulating drug does not have to go through the pulmonary circulation before it reaches the tongue, so that it gets to the tongue much more quickly. McGuire and Goldman<sup>2</sup> have reported circulation times of four seconds in cases of congenital heart disease with venous-arterial shunt. They found that the average circulation time for normal children was 10.6 seconds.

In the present case, the circulation time was normal. This factor alone should have led us to consider a diagnosis of pulmonary stenosis with closed septa. The rarity of pulmonary stenosis without a septal defect caused us to diagnose the more common condition in spite of the normal

circulation time. The fact that the circulation time was normal and that closed septa were found at autopsy suggests that measurement of the circulation time may be a valuable adjunct to the differential diagnosis of septal defects with venous-arterial shunt.

The old rheumatic deformities of the auriculoventricular valves were incidental abnormalities. Since there was no auricular dilation or hypertrophy, the valve lesions must have produced little or no functional disturbance. The acute vegetations on the pulmonary and auriculoventricular valves may have been manifestations of bacterial endocarditis. There were no clinical signs of this disease.

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## THREE CASES OF LOCALIZED GUMMATOUS MYOCARDITIS

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**I**N THE laboratory of pathology at Bellevue Hospital, in the past year, we have encountered three examples of gummata of the heart; in one of the cases there was, in addition, extensive gummatous pulmonary arteritis. Only seventeen cases of the latter disease are to be found in the literature.

There are two distinct types of myocardial syphilis, excluding the acute syphilitic myocarditis described by Warthin, about the existence of which there is a great deal of doubt, namely, diffuse and localized gummatous myocarditis.

### CASE REPORTS

**CASE 1.**—A 63-year-old white railroad worker was admitted to the Fourth Medical Division, August 9, 1940, with the complaint of progressive swelling of the abdomen for three months. For the preceding ten years he had been treated for arteriosclerotic heart disease. However, he had had no symptoms of diminished cardiac reserve until about two years before admission, when he noted some breathlessness on climbing stairs. Three months before admission he first noted swelling of the abdomen. Two months later, edema of the ankles was first noted. For ten days prior to admission his dyspnea increased markedly.

Upon admission the patient was markedly cyanotic and dyspneic, and the cervical and abdominal veins were engorged. The blood pressure was 90/70. The apex impulse of the heart was in the fourth left intercostal space outside the mid-clavicular line. The sounds were poor in quality, and the heart rate was 108. The pulmonic second sound was louder than the aortic second. There were a coarse systolic murmur at the apex and a harsh systolic murmur over the pulmonic area. Fluid was present in the abdomen.

The blood Wassermann reaction was strongly positive. An electrocardiogram revealed auricular fibrillation, coupling, and intraventricular block.

The patient grew worse rapidly, and died suddenly on the sixth day.

**Necropsy Observations.**—Necropsy was performed twenty-four hours after death. The abdomen was distended and contained 1500 c.c. of clear yellow fluid. The lower extremities were very edematous.

The pericardial sac was completely obliterated by fibrous adhesions. The heart weighed 900 grams and, in situ, presented anteriorly only the greatly enlarged right ventricle. On opening the right ventricle, we found a large, yellow, nodular mass which replaced and apparently invaded the columnae carneae and papillary muscles, and extended into the pulmonary conus, immobilizing the pulmonary leaflets and stenosing the valve. The pulmonary artery itself, for a distance of about 6 cm. from its origin, presented similar, small, scattered nodules (Fig. 1). The tricuspid leaflets were normal, but their chordae tendineae were shortened by invasion by the gummata of the corresponding papillary muscles. On section, this tissue had a bacon-like appearance. The left auricle and ventricle were moderately hypertrophied, but showed no dilatation. The mitral and aortic valves showed minimal calcification. There was no separation of the commissures of the aortic

From the Laboratories of Pathology, Bellevue Hospital.  
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valve. The coronary ostia and arteries were patent throughout. The aorta showed slight atherosclerosis.

Microscopic examination revealed that the yellow nodules consisted, at their periphery, of myocardium which was pale and poorly preserved, with moderate fibrosis and small round cell infiltration, especially in the perivascular areas. More central to this, there was a well-demarcated and unusually well-vascularized area of necrotic myocardial fibrosis, through which were scattered numerous lymphocytes, plasma cells, and occasionally multinucleated giant cells of the Langhans type.



Fig. 1.—The heart in Case 1, showing massive gummatous involvement of right ventricle and pulmonary artery.

This zone blended into a dark brown, completely necrotic mass in which no cellular structure was recognizable (Fig. 2). Levaditi's stain for spirochetes and special stains for tubercle bacilli showed nothing. Sections through the yellow nodules in the pulmonary artery revealed essentially the same histologic picture. Sections through the intervening areas revealed perivascular lymphocytic and plasma cell infiltration and vascularization of the media. The latter was indistinguishable from syphilitic mesaortitis.

Microscopic examination substantiated the gross diagnosis of massive gummatous involvement of the right ventricular myocardium and gummatous pulmonary arteritis.

CASE 2.—A 56-year-old, white woman, formerly a showgirl, was admitted October 7, 1940, to another hospital, and transferred to Bellevue Hospital three days later. The transfer summary stated that the patient had shown the signs and symptoms of congestive heart failure for one month prior to admission. Because the patient developed a psychosis, she was transferred to the Third (New York University) Psychiatric Division, Bellevue Hospital.

The previous history presented nothing worthy of note in the present connection.

The patient appeared much younger than she actually was. She was cyanotic but not dyspneic. The lower extremities were very edematous from the ankles to the knees. The liver was palpable 3 cm. below the costal margin.

The heart was enlarged. The rhythm was normal, and there were occasional premature contractions. The rate was 52 per minute, and the blood pressure, 100/60. A systolic murmur was heard over the apex and base. A superficial neurologic examination showed nothing abnormal. Psychiatric examination confirmed the diagnosis of psychosis of a type not definitely determined.

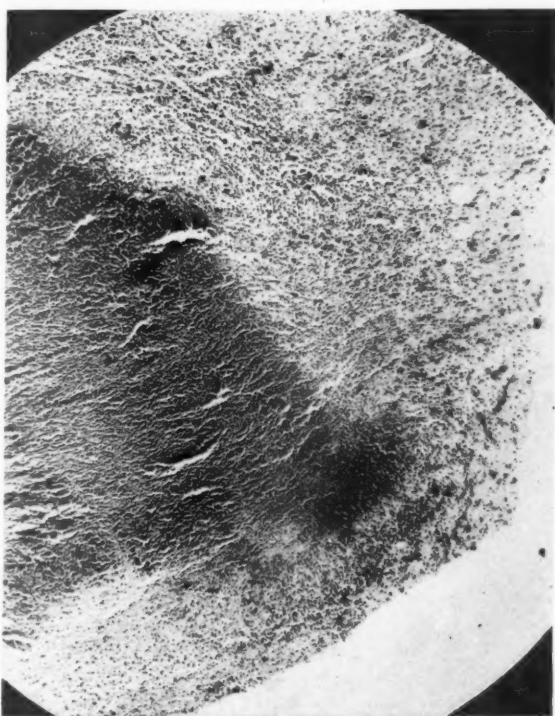


Fig. 2.—Photomicrograph of section through gumma in Case 1—H. & E., paraffin;  $\times 100$ .

The electrocardiogram showed low voltage, with auriculoventricular dissociation. The blood Wassermann reaction on admission (reported after death) was strongly positive. A roentgenogram of the chest was reported as showing cardiac enlargement in all diameters, with accentuation of all cardiac curves and obliteration of the cardiovascular angle. The other laboratory data were negligible.

The course was characterized by progressive failure and increase in stupor. The patient was treated with diuretics, sedatives, and oxygen. Thirty-six hours after admission she died; this was approximately five weeks after the onset of signs and symptoms of cardiac failure.

**Necropsy Observations.**—Necropsy was performed twenty-six hours after death. The lower extremities and subcutaneous tissues of the abdomen and chest were edematous.

The heart weighed 500 grams. The right auricular appendage contained an organized thrombus. The apex of the right ventricle adjacent to the interventricular

septum was thinned and very hemorrhagic. An organizing thrombus was attached to the endocardium in this area.

The left auricular endocardium was studded with small, smooth, rounded, firm nodules. On section they were yellowish-white and extended into the auricular wall (Fig. 3). The posterior mitral leaflet measured over 1 cm. in thickness, thus stenosing the mitral orifice. Its auricular surface presented a nodule similar to those in the auricle. It extended into the center of the leaflet, where a grayish-red

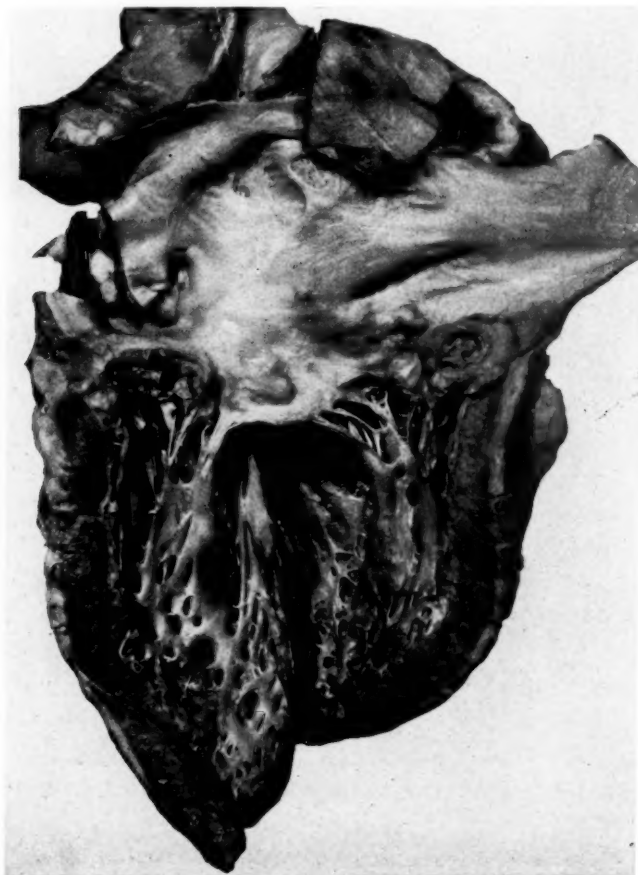


Fig. 3.—Heart in Case 2, showing multiple gummata of the left auricular wall, with involvement of posterior mitral leaflet.

necrotic mass was found, which, in turn, gradually merged with a grayish-white nodule in the left ventricular myocardium. The anterior mitral leaflet, the aortic cusps, and the coronary arteries were normal. The left ventricular myocardium revealed many small areas of fibrosis, but no nodules other than those already described.

The aorta contained numerous yellow and pearly-white plaques with wrinkling.

Microscopic examination revealed that the various nodules in the heart consisted of a central area of necrosis which gradually changed into loose connective tissue, slightly infiltrated by both large and small round cells, plasma cells, and macrophages (Fig. 4). The aorta showed thickening and fibrosis of the adventitia,

with lymphocytic and plasma cell infiltration and perivascular cuffing. The media exhibited numerous scars and vascularization, with round cell infiltration. Levaditi's stain and acid-fast stains failed to reveal either spirochetes or tubercle bacilli.

Microscopic examination substantiated the gross diagnosis of multiple gummata of the myocardium, endocardium, and mitral leaflet, and syphilitic aortitis.

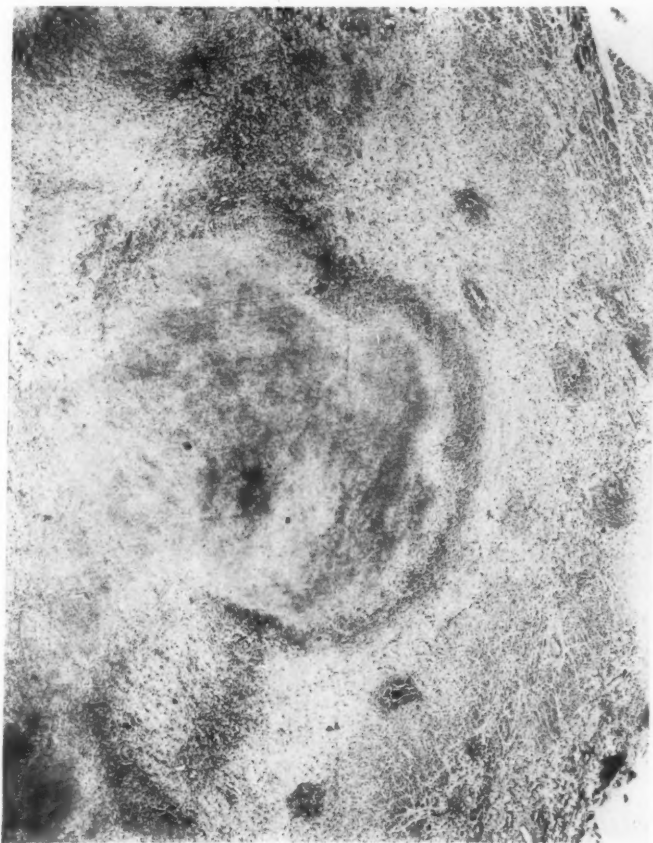


Fig. 4.—Photomicrograph through one of the gummata in Case 2. H. & E., paraffin:  $\times 100$ .

CASE 3.—A 53-year-old Greek waiter was admitted November 14, 1940, to the Third (New York University) Medical Division of Bellevue Hospital. Ten weeks before admission, the patient suddenly collapsed while walking and was unconscious for a few minutes. Similar attacks recurred twice, and, because of the frequent occurrence of dizzy spells, the patient entered another hospital. There the cardiac lesion was thought to be myocardial fibrosis, resulting in partial intraventricular heart block. The patient had had a chancre in 1922, and was treated with six injections. After the blood Wassermann reaction was found to be strongly positive, the patient was treated with intramuscular injections. Otherwise, treatment was symptomatic. After discharge from that hospital, the attacks of dizziness and syncope reappeared, and the patient was finally admitted to Bellevue Hospital.

Physical examination revealed a blood pressure of 150/62 and irregularity of the heartbeat, with a ventricular rate of 58 and a pulse rate of 42. The size of the heart was at the upper limit of normal. A systolic murmur was heard at the

apex. The second aortic sound was accentuated. The sounds were of good quality. The liver was palpable 5 cm. below the costal margin; it was smooth and not tender. The testes were enlarged to four times their normal size. They were regular in outline and very firm. The patient had moderate edema of the ankles. The leucocyte count was 10,000, and the differential count was normal. The electrocardiogram showed complete auriculoventricular block, with idioventricular rhythm.

Shortly after admission, the patient lost consciousness for fifteen seconds, ceased to breathe, and no heart sounds were audible. Gradually, cardiac contractions were resumed and the patient recovered. Thirty-six hours after admission the patient died.

A clinical diagnosis of myocardial gumma was made.



Fig. 5.—Heart in Case 3, showing a gumma in the interventricular septum.

*Necropsy Observations.*—Necropsy was performed forty-eight hours after death. Except for evidence of congestive heart failure, the relevant pathologic changes were confined to the cardiovascular system and to the right testicle.

The heart weighed 400 grams. The left ventricle was only slightly enlarged. The coronary arteries were sclerotic and their lumina narrowed. In the interventricular septum, near the base, there was an area about  $1\frac{1}{2}$  cm. in diameter which was pale yellow, in contrast to the smooth, glistening, white endocardium elsewhere. On section this lesion was found to consist of yellow-white, homogeneous, and soft but nonfriable tissue, only fairly well circumscribed, which faded gradually into normal myocardium (Fig. 5). This lesion extended through the entire thickness of the interventricular septum, sparing only the endocardium of the right ventricle. There were two other similar lesions adjacent to this one in the upper-

most part of the interventricular septum. The combined lesions involved both the membranous and muscular portions of the interventricular septum. Elsewhere the myocardium appeared normal.

The aorta showed a moderate degree of wrinkling and pearly-white elevations. The right testis was only indistinctly outlined and was surrounded by a mass of grumous, yellowish material.

Microscopic examination of the myocardial lesion showed a much thickened endocardium overlying fairly well-vascularized, loose, collagenous tissue, with some amorphous debris which resembled caseous material. The surrounding area, especially about blood vessels, was infiltrated with plasma cells, lymphocytes, and a few polymorphonuclear leucocytes. Many young connective tissue cells, with large pale nuclei, were seen (Fig. 6). The aorta showed scarring and vascularization of the media. The swelling of the right testis was identified as a gumma.

Microscopic examination confirmed the gross diagnosis of gumma of the myocardium, syphilitic aortitis, and gumma of the right testicle.

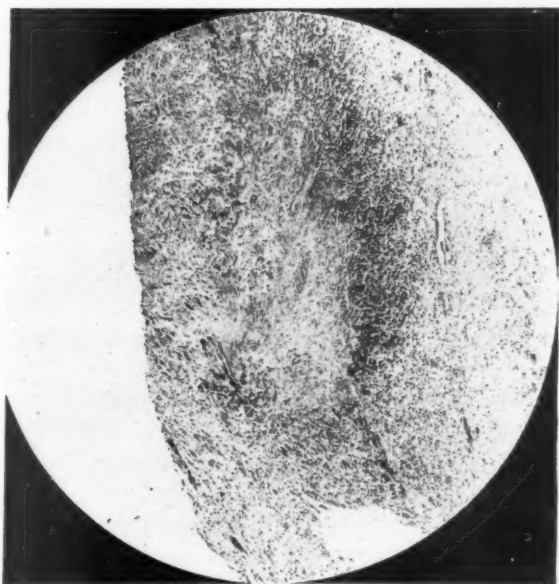


Fig. 6.—Photomicrograph of section of gumma in Case 3; H. & E., paraffin;  $\times 100$ .

#### COMMENT AND SUMMARY

Three cases of localized gummatous myocarditis are reported. The electrocardiograms in all three cases revealed conduction defects. In Case 1, the gumma impinged on both the tricuspid and pulmonary valve leaflets, producing functional impairment. In Case 2, the gummatous tissue invaded the posterior mitral leaflet and produced stenosis and insufficiency. None of the three patients presented enough clinical signs for the diagnosis of any of the commoner cardiac disorders.

Although stains for spirochetes were negative, each of the three hearts presented gross and microscopic lesions characteristic of syphilis elsewhere than in the myocardium. In addition, the blood Wassermann reaction in all three cases was strongly positive.

## ELECTROCARDIOGRAPHIC CHANGES ASSOCIATED WITH ACUTE PORPHYRIA

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THE vascular changes which occur in acute porphyria have been mentioned by several authors.<sup>1-4</sup> Hypertension and renal disease have been observed so frequently in this condition that they are considered an integral part of the syndrome, together with psychic instability,<sup>5</sup> abdominal phenomena which usually simulate mechanical ileus, neurologic changes of the flaccid paralytic variety, and porphyrin in the urine. A slight tendency toward photosensitivity may or may not be present. Waldenström<sup>1, 5</sup> stated that the renal disease and hypertension in acute porphyria are caused by arteriospasm. He described a case in which he detected angiospasm of the retinal arteries in the presence of amaurosis. In previously reported cases, sufficient coronary arterial spasm to produce anginal pain has not been noted either clinically or electrocardiographically.

The patient with whom we are here concerned had hypertension, as well as the usual neurologic, psychic, and abdominal symptoms that are associated with a severe acute attack of porphyria. There was no clinical evidence of cardiac disturbance that could be classified as congestive failure, or that suggested coronary arterial disease. The electrocardiographic changes during the acute attack and the return to normal as the condition subsided may well represent evidence that the associated coronary artery spasm was neither permanent nor the direct result of the action of that particular form of porphyrin which was detected in the urine in this case. This conclusion is supported by the observation that, in spite of the remarkable clinical improvement, relatively large quantities of the porphyrin which was present during the exacerbation were still found in the urine. Waldenström<sup>5</sup> stated that the porphyrin which is excreted in the urine is not necessarily the substance that causes the neurologic changes. It may well be that this porphyrin likewise is not the substance which causes the vasospastic phenomena.

### CASE REPORT

M. R., a white, married housewife, aged 32 years, entered the San Francisco Hospital January 11, 1939.

*Chief Complaint.*—Abdominal pain of two days' duration.

*Present Illness.*—The patient had been in the hospital on several occasions between April and December, 1938, and diagnoses of chronic alcoholism, partial bowel

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obstruction, and right ureteral stricture had been made. In December, 1938, she had been discharged after a two-day attack of fever, associated with "intestinal obstruction" of unknown etiology. Low abdominal pain, pain in the back, and anorexia had persisted.

Two days before entry on January 11, 1939, she had an attack of nausea and vomiting during which she expelled clear, mucoid material. Subsequently, sharp, cramp-like, generalized abdominal pain became evident. These symptoms persisted, with short respites. On the following day the pain radiated to the hips and the vomitus became bile-tinged.

*Family History.*—The family history was negative in regard to any illnesses that might have been manifestations of porphyria.

*Past History.*—The patient stated that sedatives, possibly of the barbitol group, had been given to her for insomnia and nervousness during a period of emotional and psychic instability before the neurologic changes had developed. In 1938, a hysterectomy had been performed. An injury sustained in childhood had resulted in blindness of the right eye.

*Physical Examination.*—The patient was a well-developed, well-nourished woman. At the time of examination she was obviously in great pain. The head and skin were normal. Anisocoria was present. The left pupil gave normal responses to light and in accommodation. The right eye showed evidences of exophoria and was blind. The nose, mouth, neck, thorax, and breasts were normal. The heart was normal except for a soft, basal systolic murmur. The peripheral vessels were palpably normal. The pressure in the brachial artery was 176/116. The pressure was equal in the two arms. The abdomen was flat and symmetrical, with a low mid-line scar; tenderness was elicited in all quadrants to deep palpation. There was no evidence of guarding, rebound phenomenon, or ascites. Borborygmi were normal. The muscular development of the extremities was normal and no wasting was noted. Normal reflexes were obtained bilaterally. Sensation to touch was slightly diminished below the knees. The psychiatrist who examined the patient suggested that the recurrent, unexplained, abdominal pain might be caused by psychic trauma, and that the patient might be addicted to narcotics.

*Laboratory Examination.*—Urine analysis on January 12, 1939, disclosed a clear amber color; a pH of 5.5; a specific gravity of 1.024; a slight trace of albumin; no reducing substances; a few hyaline casts; and 3 erythrocytes to each high dry field. The hemoglobin value was 84 per cent on the Sahli scale, with 4,470,000 erythrocytes per cubic millimeter. There were 6,800 leucocytes per cubic millimeter, 71 per cent of which were neutrophils and 8 per cent eosinophilic polymorphonuclear cells. The blood Wassermann reaction was negative. The radiologic report was as follows: "There is a minimal gaseous dilatation of the colon, no evidence of intestinal obstruction or opaque calculi." Excretion pyelograms showed "poor filling of the left kidney probably due to spasm but no evidence of pathologic findings in the genitourinary tract." The skull also was normal radiologically.

*Course.*—On January 30, 1939, the patient complained of inability to use her hands, arms, and legs. Neurologically, her condition was said to resemble astasia abasia. Lumbar puncture revealed no abnormalities of either pressure relationships or chemical content of the spinal fluid. The urine for the first time was of a reddish-amber color, and the hemoglobin had dropped to 59 per cent (Sahli).

Two days later the patient was transferred to the psychiatric service. A central type of facial palsy, vertical nystagmus, a generalized flaccid paralysis of the extremities, and a decreased response to faradic stimulation were noted. The sensations were normal. Laryngeal paralysis, muscular pain, and hyperesthesia subsequently developed. Trichinosis and periarteritis nodosa were suspected, but biopsy of the pectoral muscle was negative for both encysted trichinae and arterial changes. The precipitin test for trichinosis was negative also. The fasting blood urea nitrogen was 47 mg. per cent. The electrocardiogram is presented in Fig. 1.

Four months later, on May 9, 1939, the patient was transferred to the Laguna Honda Home Infirmary. Her physical and mental status was but slightly changed. Later it was evident that atrophy of the muscles of the hands, legs, and arms was becoming progressively more severe. Left lateral nystagmus was demonstrated. The deep tendon reflexes were absent. No sensory changes had occurred. In October, 1939, dysphagia, with nasopharyngeal regurgitation of food, and dysarthria occurred. Subsequently, evidences of aspiration pneumonia were noted. It was at this time that the diagnosis of acute porphyria was made and proved by spectroscopic identification of porphyrin in the urine. Therapy was instituted with calcium and vitamins (including vitamins A, B, C, D, and G, but excluding vitamin



Fig. 1.—Electrocardiogram recorded February 25, 1939. The patient manifested the neurologic changes noted in the case report, as well as hypertension and renal disease. Apparent are sinus tachycardia, marked elevation of the S-T segment in Lead I, diminished voltage of the major deflections, and left axis deviation. Lead IV is the IV-F of the Committee on Precordial Leads of the American Heart Association.

E) in large doses (especially the vitamin B complex). Iron and liver extracts were administered both orally and parenterally. As no improvement had occurred on this regime after four months, the administration of alpha tocopherol was begun April 26, 1940, and all other medication was discontinued. The results are noted in Fig. 2. This form of therapy has been continued to the present time. The patient is continuing to improve. Her motor power has increased so that she can walk unsupported. Her mental aberration no longer exists; she is remarkably

stable emotionally, and has acute insight, especially in regard to the periods of alcoholism and psychic instability which were prominent at the onset of the illness. Wrist and ankle drop of moderate degree persist. Bulbar disease is not evident. All deep tendon reflexes are obtainable. No reaction of degeneration can be dem-

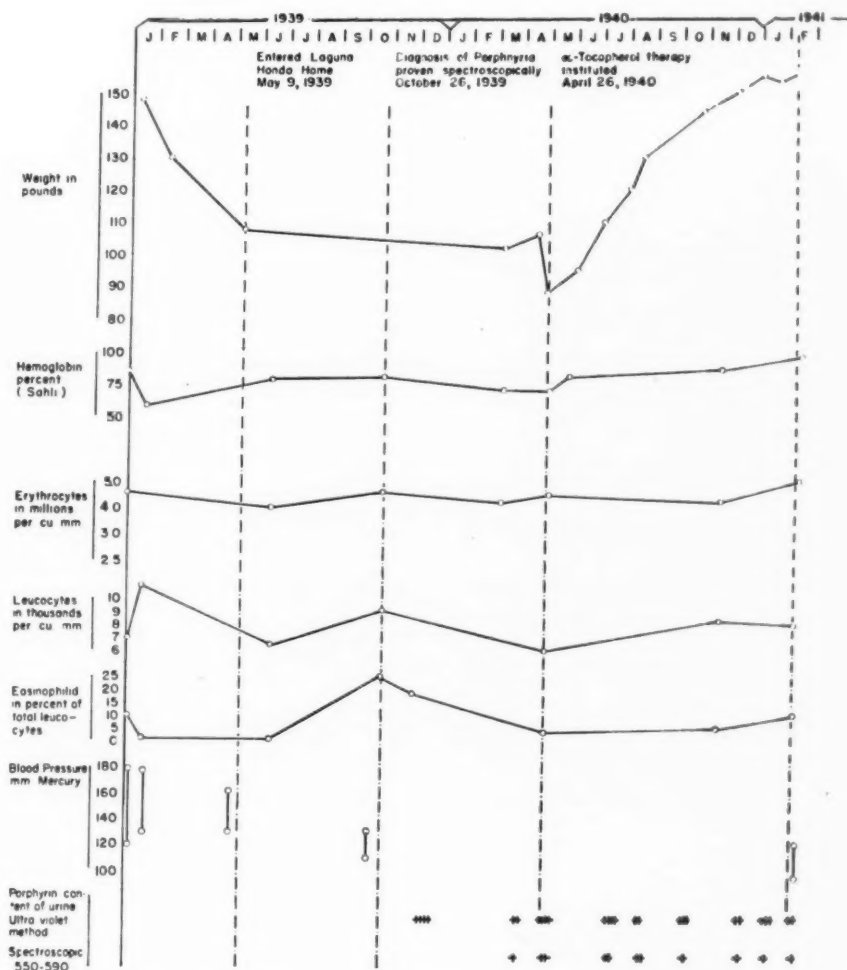


Fig. 2.—Graphic representation of the clinical course in a case of acute porphyria, showing the remission which occurred coincidental with the administration of alpha-tocopherol.

onstrated. Her weight is 152 pounds; the hemoglobin and erythrocyte count are normal; the blood pressure is 122/76. The porphyrin content of the urine is shown in Fig. 2. An electrocardiogram taken June 28, 1940, two months after she began to improve, is shown in Fig. 3, and another, taken February 24, 1941, is shown in Fig. 4.

#### DISCUSSION

The electrocardiographic abnormalities at the onset of the exacerbation were in all probability the result of coronary arterial spasm, and

strongly suggest that the acute attack was associated with transient anterior coronary artery disease. Judging from the reports of others who have recorded electrocardiographic changes in acute hypertensive states,<sup>6</sup> we conclude that hypertension alone could probably not produce such changes. The abnormalities in the electrocardiogram consist principally of elevation of the S-T segment in Lead I and slurring of the S-T segment in Lead III. Elevation of the S-T segment in Lead I is certainly not the usual result of uncomplicated hypertension.

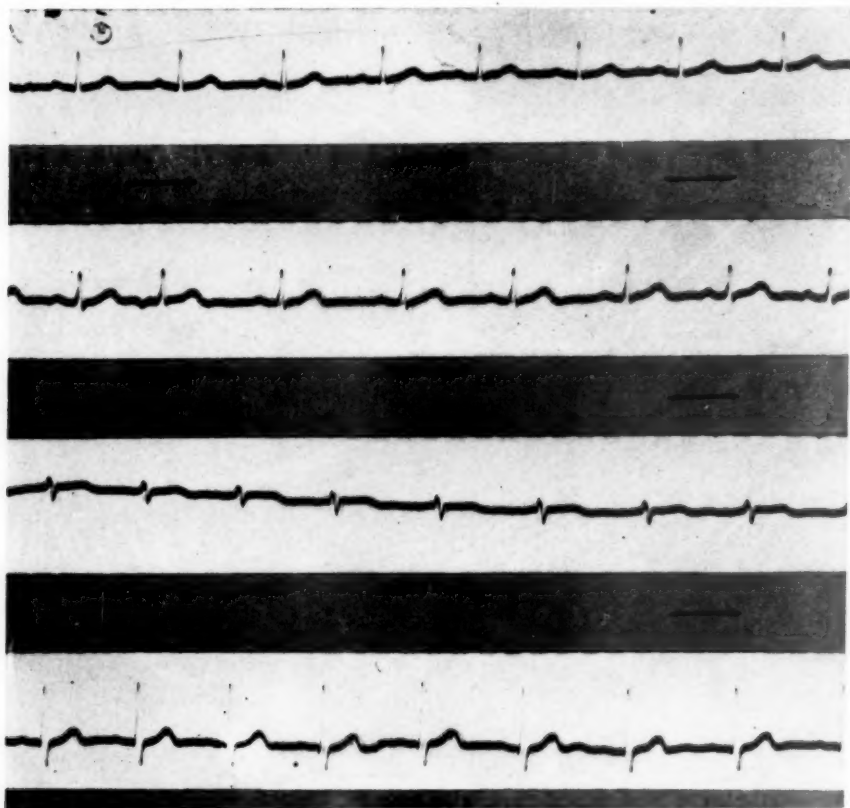


Fig. 3.—Electrocardiogram recorded June 28, 1940, during the period of remission, without hypertension or evidence of renal disease. The rate is 80 per minute, the S-T segment in Lead I is normal, and the voltage of the major deflections is increased.

Whether the hypertension in acute porphyria is the result of renal ischemia, peripheral vasomotor changes, or both, has not yet been ascertained. The electrocardiographic changes are apparently caused by transient myocardial ischemia, rather than actual cardiac infarction. They are evidently the result of coronary arterial spasm, which is but one aspect of the general phenomenon of angiospasm—probably the fundamental physiologic derangement in acute porphyria.

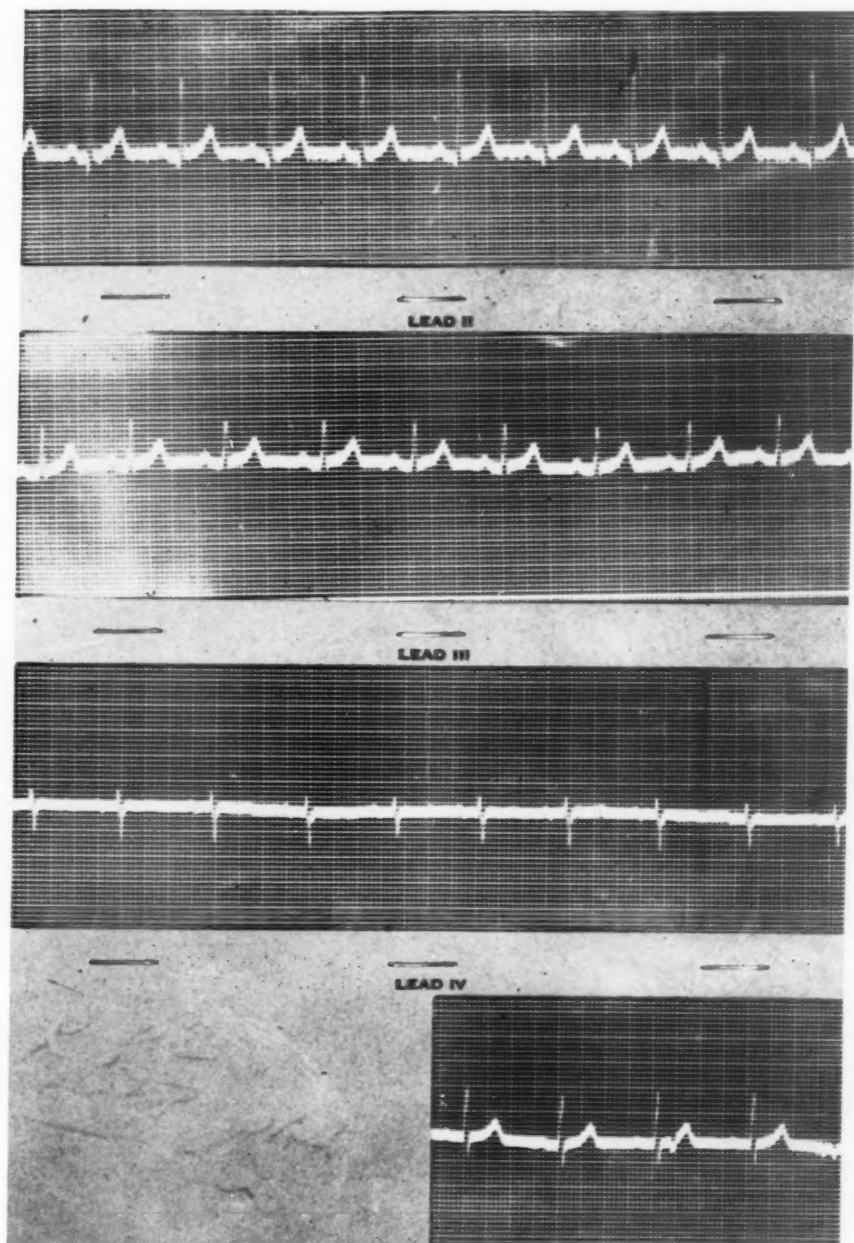


Fig. 4.—Electrocardiogram taken February 24, 1941, during the period of continued improvement. The axis deviation remains to the left, the voltage has increased to normal, and the S-T segments have returned to normal.

## SUMMARY

The clinical report of a patient who was observed in an exacerbation and remission of acute porphyria is presented.

The electrocardiographic changes that occurred suggest that the angiospasm which is known to be an outstanding phenomenon in this disease involves the coronary arteries as well as other blood vessels.

The reversion of the electrocardiogram to normal with the subsidence of the syndrome was sufficiently well defined to warrant the conclusion that the vasospasm is of a transient nature and does not produce permanent myocardial disease.

We are grateful to Dr. Gordon E. Hein for his guidance and for the spectroscopic determinations of porphyrin in connection with this case.

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## TRAUMATIC RUPTURE OF THE RIGHT VENTRICLE AN UNUSUAL CASE

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IN 1935, Claude S. Beck<sup>1</sup> reviewed the subject of contusions of the heart and outlined the following mechanisms by which rupture of a heart takes place as a result of nonpenetrating forms of trauma to the chest.

1. Contusion of the heart, with subsequent softening. This softening is usually greatest during the second week, and there is the possibility of cardiac rupture at that time.

2. Increasing intracardiac pressure by the application of compression force to the legs or abdomen.

3. Broken ribs driven into the heart.

4. Bursting the heart by compression between sternum and vertebrae.

In the same year, Bright and Beck<sup>2</sup> completely reviewed 152 cases of cardiac rupture in the literature up to that time, and cited only one in which rupture was caused by compression of the heart between the sternum and spine; this would fall into Group 4, as outlined above. Review of the literature since then shows no similar case.

### CASE REPORT

S. E., a well-nourished and well-developed white boy (age, 12 years; height, 5 feet 2 inches; weight, 145 pounds), had always been well except for measles. There was no history of rheumatic fever, syphilis, or congenital cardiac anomaly.

On February 1, 1941, he was riding on a sled, face down. The sled was tied to the rear of an automobile and was being pulled at a slow speed for the pleasure of the boy. A companion jumped directly on him to share the ride. He flung himself lengthwise on the boy as children often do. The latter let out a peculiar noise that alarmed the lad on top of him, and he, in turn, called on the driver of the car to stop. When they looked at the victim he was quiet and nonresponsive. They immediately rushed him to the hospital, where the intern (one of us, E. R.) pronounced him dead.

Autopsy was performed by Dr. William C. Wilentz. External examination revealed the following significant points. The body was flaccid and cold. The lips were cyanotic. There was a 3 inch by 1 inch brush abrasion contusion mark over the right anterior portion of the chest wall at the level of the nipple and to the right of the sternum. There was no further evidence of external injury or violence. Internal examination revealed no evidence of any fracture of the ribs, but slight hemorrhage was present in the intercostal tissues directly underneath the external contusion abrasion. The right lung was normal. The left lung was normal in size, but the lowermost part of the lower lobe was severely contused, and, on section, showed much hemorrhage. The pericardial sac was tremendously distended

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with free and clotted blood. The right ventricle was ruptured throughout its entire length (Fig. 1). The heart was otherwise normal. The liver, spleen, and kidneys were normal in size and appearance, but showed mild congestion. The remaining viscera and cavities were normal.

It was evident that the child had died immediately of cardiac tamponade caused by rupture of the right ventricle.

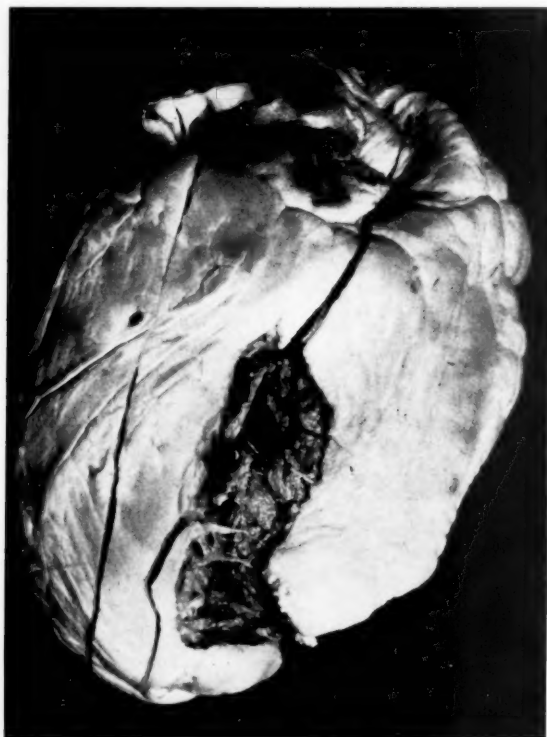


Fig. 1.—Traumatic rupture of the right ventricle.

#### COMMENT

Bright and Beek,<sup>2</sup> Hawkes,<sup>3</sup> and Barber<sup>4, 5</sup> call attention particularly to the fact that living cardiac muscle is very susceptible to rupture by abnormal external forces. No one part of the heart is injured more than any other, when all of the reported cases are considered.

The cause of the death of this child was no doubt the same as in most other cases. The compressive force was probably applied to the chest when the cardiac cycle was at the end of diastole or beginning of systole, when the heart was filled with blood. If, in addition, the glottis happened to be closed and the chest was in the inspiratory phase, conditions for transmission of the compressive force from the chest to the heart would be particularly favorable.

It seems to us that the right ventricle ruptured in this particular instance because its wall is thinner than that of the left ventricle.

## SUMMARY

A case of complete rupture of the right ventricle, resulting in hemo-pericardium, cardiac tamponade, and immediate death, is reported. The rupture was caused by the application of a sudden compressive force to the chest.

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## Abstracts and Reviews

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### Selected Abstracts

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**Schroeder, H. A.: Arterial Hypertension in Rats. I. Methods. J. Exper. Med. 75: 513, 1942.**

Normal standards for the blood pressure of rats under pentobarbital sodium anesthesia have been ascertained. Arterial hypertension did not consistently follow the injection of estradiol and pitressin in adult rats, and only transient hypertension occurred after the injection of dihydroxyphenylalanine. The injection of adrenalin in oil, however, was followed by cardiac hypertrophy, and it also resulted from (a) partial constriction of one renal artery, (b) the production of unilateral hydro-nephrosis, (c) traumatic injury to one kidney, (d) inducing unilateral perinephritis with a cellophane membrane. The blood pressure in many of the animals became elevated.

In rats the weight of the heart is probably a more reliable index of the presence of the hypertensive state than is one measurement, or two, of blood pressure under anesthesia. The latter is extremely variable, both in normal and in hypertensive animals. Rats are, however, liable to hypertension under natural circumstances, and it can be easily induced in a number of ways. The weight of the heart may then become rapidly increased. To judge from the findings in this species, rats are very susceptible to the production of the hypertensive state, in comparison with other animals.

AUTHOR.

**Wolferth, C. C., Livezey, M. M., and Wood, F. C.: Studies on the Distribution of Potential Concerned in the Formation of Electrocardiograms. Am. J. M. Sc. 203: 641, 1942.**

Electrocardiograms made between small areas situated along a line drawn from the  $C_1$  position to the tip of the right acromion (the right arm being regarded as an electrically intermediate position between the tip of the acromion and the axilla) all show a ventricular contour similar to Lead  $CR_1$ , provided the same polarity is used in all these leads as in  $CR_1$ . This we have called the  $C_1$  pattern of potential. The size of the deflections seems to be related to the potential variations at the  $C_1$  position; the distance of the paired areas from the heart; and their distance from each other.

Electrocardiograms made between small areas situated along a line drawn from a position slightly outside the cardiac apex to the tip of the left acromion (the left arm being regarded as an electrically intermediate position between the tip of the acromion and the axilla) all show a ventricular contour similar to that of the CL lead made to the position just outside the cardiac apex, provided the same polarity is used in all these leads as in the CL lead. This we have called the  $C_s$  pattern, although it may be derived from the  $C_4$  or  $C_6$  position, depending on the relation of the cardiac apex to the chest wall. The size of the deflections seems to be related to the potential variations at the  $C_s$  position; the distance of the paired areas from the heart; and their distance from each other.

By pairing appropriate areas along each of these two lines and making electrocardiograms with the same polarity as in Lead I, a series of tracings closely resembling Lead I can be obtained. The deflections become larger as the paired areas approach the  $C_1$  and  $C_5$  positions.

Various combinations of three positions can be found along each of these two lines whose relationships are such that the ventricular potential of the intermediate position is approximately equal at all instants to the mean of the ventricular potentials of the proximal and distal positions.

The above-mentioned findings suggest that there is marked decrement in the  $C_1$  pattern between the  $C_1$  position and the right shoulder and also marked decrement in the " $C_5$  pattern" between the position just outside the cardiac apex and the left shoulder. However, there appears to be very little alteration in contour of either pattern along these radial lines from the precordium to shoulder tip.

By methods described in the text, combinations of three positions can be found along each of the two lines, whose relationships are such that the sum of the ventricular potential of the area nearest to the heart along one line plus that of the two areas farther from the heart on the other line is approximately equal at all instants to the sum of the potentials of the other three areas. Furthermore, when such positions have been found, the relationships of the three areas on each side are such that the potential of the proximal area minus the sum of the potentials of the two distal areas on one side is approximately equal at all instants to the potential of the proximal area minus the sum of the potentials of the two distal areas on the other side.

On the basis of the above-mentioned relationships, the following may be demonstrated:

1. Lead I can be reproduced by the application of electrodes to various combinations of four chest positions without electrodes on either arm.

2. Either the  $C_1$  pattern of potential is almost completely responsible for the potential variations of the right arm and the " $C_5$  pattern" of potential is almost completely responsible for the potential variations of the left arm, or else there is an additional pattern of potential variation common to all these areas which is not reflected in the tracings because it is identical at areas so near the heart as the  $C_1$  and  $C_5$  positions, and so far away as the right arm or tip of the right shoulder and the left arm or the tip of the left shoulder.

3. No matter which of the above alternatives is correct, Lead I represents the subtraction of the  $C_1$  pattern of potential variation after it has undergone decrement, from the " $C_5$  pattern" after it has also undergone decrement.

4. If the first alternative stated above in "B" is correct, a method can be devised for recording the potential variations of the ventricular origin in a single area. If the second alternative is correct, the method as described records the potential variations of a single area minus the hypothetical concealed pattern of potential common to all the areas mentioned in "B." Thus, no matter which alternative is correct, the study of potential patterns can be simplified by the elimination of the obscuring effects of the  $C_1$  and " $C_5$  patterns" present in upper parts of the body.

The presence of the  $C_1$  and " $C_5$  patterns" of potential can be demonstrated below the diaphragm by appropriate methods. No test was made for other anterior chest patterns. The rather scanty evidence now available, however, indicates that a pattern or patterns of potential which seem to exert comparatively feeble effects above the diaphragm (at least in the formation of the  $C_1$  and  $C_5$  patterns) influence greatly either the potential variation of the lower part of the body or the hypothetical concealed potential not subject to the decrement in the upper part of the body. From the practical point of view it would appear to make little difference which of these alternatives is correct.

Limited studies of the lower esophageal pattern of potential (below the level at which the electrode is in close contact with auricular muscle) suggest that the part of the heart responsible for this pattern has a marked effect on the form of the ventricular electrocardiogram when an area above the diaphragm (at some distance from the precordium) is paired with an area below the diaphragm.

The pattern of esophageal potential, at and above the level where the electrode is in close proximity to auricular muscle, resembles that which has been described as the endocardial pattern of potential variation more closely than it resembles the epicardial pattern. The effects of this pattern are probably not entirely negligible on the body surface.

The relationships among potential differences on the body surface resulting from cardiac electrical activity appear to be different from what Einthoven conceived them to be when he formulated the equilateral triangle hypothesis. The demonstration that certain patterns of potential variation found to exist in positions near the heart remain intact in positions far from the heart, except for decrement, and the relationships discovered as a result of these phenomena indicate the necessity for reconstructing electrocardiographic theory. An attempt has been made to begin this reconstruction.

AUTHORS.

**Öhnell, v. R. F.: Concerning Paroxysmal Tachycardia: Two Families in Whom an Inclination to Heart Failure and Fixed Changes in the Electrocardiogram Were Constant.** *Cardiologia* 5: 326, 1941.

Two families with disposition to heart attacks have been described (frequency-changes, sensorial symptoms in the heart region, almost unconsciousness, polyuria, etc.—these symptoms combined or single). In the electrocardiogram between attacks, there is often a gradual rise of the initial part of the QRS-complex. Other electrocardiographic changes are also described. The possibility that we are dealing here with one and the same hereditary disease has been discussed.

Apparently, paroxysmal tachycardia may be due to hereditary causes.

AUTHOR.

**Perera, G. A., Levine, S. A., and Erlanger, H.: Prognosis of Right Bundle Branch Block: A Study of 104 Cases.** *Brit. Heart J.* 4: 35, 1942.

An analysis of 104 cases of right bundle branch block has been prepared.

It was observed that reduplicated heart sounds, gallop rhythm, and pulsus alternans were uncommon in this series. The two latter disorders were noted in a small group that had advanced heart disease.

Forty per cent of the patients had no appreciable subjective discomfort from the heart. In fact, some have no subjective or objective evidence of heart disease apart from the right bundle branch block.

The average survival time after the diagnosis of right bundle branch block of 29 fatal cases, was three years. If the 6 cases that came into the hospital more or less moribund and died within a few days are excluded, the average survival period of the fatal group was four years and five months. Of the 62 patients alive when last seen or heard from, the average survival period was four years and one month. The longest survival period amongst the living cases was seventeen years, and amongst the fatal cases, sixteen years and seven months.

The clinical impression that patients with right bundle branch block have a distinctly more favorable prognosis than do those with a left bundle branch lesion has been sustained.

AUTHORS.

**Campbell, M.: Inversion of T Waves After Long Paroxysms of Tachycardia.** Brit. Heart J. 4: 49, 1942.

After long paroxysms of tachycardia the T waves may become inverted in one or more leads for some days. This does not indicate any organic disease, but is a completely reversible process indicating some degree of exhaustion or strain of the heart muscle.

AUTHOR.

**Stein, W., and Uhr, J. S.: Congenital Heart Block: Report of a Case.** Brit. Heart J. 4: 7, 1942.

Complete heart block represents an inability of the stimulating impulses originating in the sino-auricular node to pass through the auriculoventricular node and the main bundle of His, so that the auricles beat at their own rate while the ventricles contract at the rate governed by the auriculoventricular node that has taken over the function of pacemaker, which is usually 30 to 50 beats a minute, or if conduction from the latter is impaired also, then at their own ventricular rate, which is usually below 40 beats per minute. This heart block may be congenital, which is rare, or acquired, which is more usual.

Yater (1929) reviewed 30 cases of congenital heart block reported up to that time, and established certain criteria that would permit one to classify a case as being congenital. These were the following five points:

1. Electrocardiographic evidence of the block existing.
2. A slow pulse that had been found present at an early age and had continued to be present.
3. The absence of any history suggestive of an infection that might have produced the block, as diphtheria, congenital or early acquired syphilis, rheumatic fever, or chorea.
4. A history of any one of the following: syncopal attacks, fainting spells (explained on the basis of the Adams-Stokes syndrome), vertigo, headaches, nausea and vomiting after unusual exertion, convulsions, dyspnea, and/or cyanosis. (These findings may or may not be present and are not absolutely requisite for the criteria, but if present add further evidence.)
5. The presence of a congenital heart lesion, namely, patent interventricular septum (the latter at times being subject to an acquired endomyocarditis, quite infrequent in this instance as far as the septum itself is concerned).

While theoretically it might be possible to explain the heart block on a prenatal myocarditis or syphilis involving the bundle of His or a developmental defect affecting the bundle of His, these are most unlikely to occur for practical considerations.

This case fits the criteria of Yater (1929).

The etiology of congenital heart block is organic and is based on the pathological presence of a patent interventricular septum. Such septal defects, both large and small, are a common deformity and are found relatively frequently. Why they occur clinically without the presence of heart block so often, is odd, but has been explained correctly as follows: The usual site of the interventricular defect is anterior to the pars membranacea while the A-V bundle lies behind it (Leech, 1930). Inasmuch as the ventricular complexes in the electrocardiogram of complete heart block are normal, it follows that the lesion responsible for the block must be in the course of the main bundle of His, above the bifurcation close to the septum (Lampard, 1928).

The reason for the almost constant preservation of the muscular connection between the auricles and ventricles probably lies in the fact that the special bundle ap-

pears in the fifth week of fetal life, whereas the membranous separation between auricles and ventricles take form between seven and ten weeks. The bundle is preserved between the posterior endocardial cushion and the posterior portion of the annular fibrosis (Yater, Leaman, and Cornell, 1934; Moll, 1912; and Tandler, 1913).

It is only when the A-V node or main bundle of His is caught in the congenital anomalous development of the septum, or is caught in the excessive formation of fibrous tissue of the membranous portion of the septum interfering with the continuity of the bundle, that heart block occurs (Aitken, 1932).

The prognosis in general is guarded. A few cases have reached mature adult life. It must be remembered that a patent interventricular septum is associated often with other congenital cardiac anomalies, the most frequent being the tetralogy of Fallot. These anomalies are overshadowed by the dangers of an engrafted endocarditis. If the concomitant anomalies are small and do not limit the functional capacity of the heart permitting the subject to survive early life, there is no reason to consider the prognosis unfavorable, barring an unlooked-for bacterial endocarditis.

AUTHORS.

**Van Bogaert, A., and Van Baarle, F.: Contribution to the Study of Arterial Hypertension in Connection With the Hypothalamo-Hypophyseal System. *Cardiologia* 5: 273, 1941.**

Starting with the conclusions of a former paper dealing with the role of the hypothalamus in the genesis of a chronic arterial hypertonia, comparable to essential hypertonia in man, the authors have explored the eventual role of the hyperactivity of the hypophysis and the normal secretion of the hypophysis on exciting the hypothalamic centers and tracts. After a critical study of the biological signs of a hyperactivity of the hypophysis in the case of essential hypertonia, the authors come to the following conclusion: The freeing of the encephalobulbic sympathetic pressure centers determines on the one hand the arterial hypertonia and on the other a hypersecretion of the hormones of the hypophysis. Many animal experiments enabled the authors to prove this hypothesis. The presence of hypophysis hormone in larger quantities than the normal in the biological fluids in no way allows one to conceive a causal connection between the secretion of the hypophysis and the increase in the blood pressure, since both are the independent consequences of an excitation of the sympathetic encephalobulbic centers, amongst them that of the hypothalamus.

AUTHORS.

**Marvin, H. M.: The Diagnosis of Coronary-Artery Disease. *New England J. Med.* 226: 251, 1942.**

The clinical evidence that points to coronary arteriosclerosis consists of a clear history of anginal heart failure in the absence of the other infrequent causes, the occurrence of acute myocardial infarction, or the presence of congestive heart failure if other types of heart disease and vitamin deficiency can be excluded.

The roentgenologic evidence of coronary arteriosclerosis is present if calcification of the vessels can be demonstrated, if there is a ventricular aneurysm, or if localized reversal of ventricular pulsation is revealed by fluoroscopic examination.

If myocardial infarction is excluded, there is no change in the electrocardiogram that in itself justifies the diagnosis of coronary disease, because the alterations on which this diagnosis is based may be—and often are—due to other causes.

AUTHOR.

**Lisa, J. R., Magiday, M., and Hart, J. F.: Peripheral Arteriosclerosis in the Diabetic and Nondiabetic: A Study of One Hundred and Six Amputated Legs. J. A. M. A. 118: 1353, 1942.**

The peripheral vascular pathologic condition of 109 amputated legs was studied. There were 56 diabetic specimens and 53 nondiabetic specimens. The two types were in the same age period. The women outnumbered the men in the same diabetic group. The opposite was true in the nondiabetic group. The arterial changes were similar in the two groups. Acute venous occlusions and phlebosclerosis were more frequent among the nondiabetic. Infection with cellulitis was only slightly more frequent in the diabetic group. Dry gangrene occurred almost as frequently in the diabetic as in the nondiabetic. The occlusive element in arteriosclerosis is the dangerous feature in both types. The terms dry and wet gangrene do not properly describe the conditions found. More rigid criteria and more careful differentiation between the lesions secondary to occlusive arterial disease and those due to infection should be instituted.

AUTHORS.

**Harkins, H. N., and Schug, R.: The Surgical Management of Varicose Veins: Importance of Individualization in the Choice of Procedure. Surgery 11: 402, 1942.**

In a series of varicose vein operations personally conducted on 98 extremities of 63 patients during 1940, 217 incisions and 19 strippings were done.

A stereotyped operation should be avoided. The surgical procedure should be individualized to fit the patient and to block all important venous incompetencies as determined by complete diagnostic tests.

High ligation and segmental excision of the saphenous vein and all its branches at the fossa ovalis should be performed in all cases submitted to surgery.

Additional ligations and excisions lower down on the thigh or leg should be performed as indicated.

Stripping gives a better cosmetic result than excision and is preferable to the latter except in cases of superficial, friable, or recently sclerosed veins and for veins high in the thigh.

Injection as an adjunct to surgery is best postponed until the second week after operation.

Important points in the surgical technique include the use of local anesthetic, silk, transfixion of main vessels, elastoplast bandages, and ambulatory cure in all cases.

The one ill effect of consequence in these cases was a slight increase in the edema of one leg in two cases and a marked edema in another case.

AUTHORS.

**Bosse, M. D., and Strang, J. M.: Chronic Occlusion of Portal Vein: Report of Two Cases, One a Case of Occlusion Associated With Aneurysm of the Splenic Artery and Carcinoma of the Liver (Hepatoma). Arch. Path. 33: 372, 1942.**

Two cases of chronic occlusion of the portal vein by calcific thrombi are reported. One of the patients was a white man 58 years old. The occlusion was associated with aneurysm of the splenic artery and hepatoma of the liver. The portal thrombosis in this case was probably secondary to acute appendicitis. The thrombosis involved tributary and dilated collateral veins as well as the main portal stem. The other patient was a white man 38 years old. The occlusion may have resulted indirectly from mitral stenosis. Both patients had sclerosis of the portal system.

The aneurysm of the splenic artery was of the cirroid type. The hepatoma was associated with portal cirrhosis. Only one report of chronic portal occlusion associated with aneurysm of the splenic artery was found in the literature. Association of primary carcinoma of the liver with either chronic portal occlusion or aneurysm of the splenic artery was not found.

AUTHORS.

**Altschule, M. D., Gilligan, D. R., and Zamcheck, N.: The Effects on the Cardiovascular System of Fluids Administered Intravenously in Man. IV. The Lung Volume and Pulmonary Dynamics. J. Clin. Investigation 21: 365, 1942.**

Studies of the effect of the injection of fluids intravenously on the subdivisions of the lung volume and on the respiratory dynamics have been made in six normal subjects.

Injection intravenously of 1800 c.c. of isotonic sodium chloride solution, at rates of 39 to 185 c.c. per minute, in these normal subjects caused no change in residual air, and only slight decreases in the vital capacity, its components, the reserve and complementary airs, and in the total lung volume. The respiratory minute volume showed no consistent change, although the tidal air was usually decreased. All the changes in pulmonary function found after intravenous infusions in these normal subjects were insignificant.

The slight decreases in vital capacity, its components, and the total lung volume, after these massive intravenous infusions at rapid rates in these normal subjects, are interpreted as due to slight pulmonary vasodilatation associated with temporarily increased blood volume.

The fact that changes in pulmonary dynamics and lung volume, following rapid intravenous injections of large volumes of fluid in normal subjects, were at most only slight, in no way alters the clinical concept that when it is necessary to administer fluids intravenously in patients with a tendency toward pulmonary congestion and edema, because of cardiac, pulmonary, central nervous system, or renal disease, these infusions should be given at slower rates and with caution.

AUTHORS.

**Battro, A., and Labourt, F. E.: Contribution to the Study of Functional Pulmonary Capacity in Certain Cardiopathies (Method of Spirography). Rev. argent. de cardiol. 8: 317, 1941.**

The functional pulmonary capacity of 30 cardiac patients was measured by determining the oxygen consumption and respiratory volume while breathing air or oxygen, during rest and during exercise. The criteria adopted for the classification in 4 degrees of respiratory insufficiency are described.

Eighteen of the 30 patients had mitral stenosis; the other 12 had various heart diseases with manifest signs of left ventricular failure.

In the rest, 73.3 per cent of the patients showed no sign of functional pulmonary insufficiency.

During exercise an arterial unsaturation of oxygen was manifested in 66.6 per cent of the patients.

The causal factors in the respiratory insufficiency of cardiac patients are discussed.

AUTHORS.

**Cournand, A., Ranges, H. A., and Riley, R. L.: Comparison of Results of the Normal Ballistocardiogram and a Direct Fick Method in Measuring the Cardiac Output in Man. J. Clin. Investigation 21: 287, 1942.**

The accuracy of the ballistocardiographic method of cardiac output determination was tested by comparing it with a method based on the Fick principle.

The technique of the direct Fick determination, involving catheterization of the right auricle, was discussed.

Fourteen almost simultaneous pairs of cardiac output determinations were compared, in which the following criteria were satisfied: pulse rate varied less than 4 beats; ballistocardiograms were normal in shape, regular, and easily readable; cardiac output calculated separately from oxygen consumption and from carbon dioxide elimination checked closely.

Cardiac output as determined by the direct Fick method was found to be larger by 18.5 per cent than the value calculated from the ballistocardiogram, using Bazett's tables for internal cross-section of the aorta.

Using figures for aortic cross-section obtained by diodrast visualization in 5 cases, cardiac output as calculated from the ballistocardiogram was found to check very closely with the values obtained by the direct Fick method, the average difference being 3.5 per cent.

On the basis of these findings, it is suggested that the accuracy of cardiac output determination with the ballistocardiograph may be improved by correcting the calculated value by an amount equal to the average error found experimentally, i.e., 18.5 per cent, or by introducing in the formula a value for internal cross-section of the aorta on diodrast visualization.

AUTHORS.

**Kerwin, A. J.: Pulmonocardiac Failure as a Result of Spinal Deformity: Report of Five Cases. Arch. Int. Med. 69: 560, 1942.**

The clinical and pathologic characters of 5 cases of pulmonocardiac failure in extreme spinal deformity are described.

The significant pathologic lesions are the result of pulmonary hypertension, which eventually leads to right-sided heart failure and appears to be due to mechanical interference with respiratory function.

AUTHOR.

## Book Reviews

**ELECTROCARDIOGRAPHY:** By Louis N. Katz, M.D., Director of Cardiovascular Research, Michael Reese Hospital, and Assistant Professor of Physiology, University of Chicago. Lea and Febiger, Philadelphia, 1941, 580 pages, 402 illustrations, \$10.00.

This book is not a compilation of the accumulated knowledge on the subject but is more especially an expression of the opinions of the author. It seems at times that the author's observations and hypotheses are given undue prominence when one considers the wide scope of the literature with its divergent opinions. His opinions are frequently at variance with widely accepted hypotheses and diagnostic classifications, and one does not always feel that the reasons for thus diverging from the generally accepted views are compelling. Several features particularly attract the attention of the reviewer because they seem to represent a backward step in the study and interpretation of the electrocardiogram. In discussing the QRS group the author writes practically a new nomenclature and lists seven different varieties of QRS. He recommends dropping the term "axis deviation" and introduces in its place two other terms. The diagnostic distinction made between the records which are said to indicate "axis shift" and those indicating "ventricular preponderance" does not rest upon any experimental evidence and is, in fact, little more than a hypothesis.

There are a surprising number of records with very slight and seemingly insignificant variations from the normal which are considered by the author as "definitely abnormal" or as "borderline"; such, for instance, are Figs. 94 B, 94 C, 72 A, and 209 B. There is doubt whether what is here called progressive chronic coronary insufficiency should not be called progressive myocardial degeneration. The myocardium is nearer to the electrocardiogram than the coronary arteries are, and it is quite possible to name conditions other than coronary disease that might be responsible for the electrocardiographic changes in question. There is considerable doubt whether such diseases as pericarditis, pulmonary embolism, uremia, cardiac trauma, severe acute anemia, and dissecting aneurysm should be regarded as affecting the electrocardiogram by the mechanism of coronary insufficiency. There is no question that these conditions are often associated with abnormalities of the waves, but here again it is the myocardium which influences the record, and it is probably this that is primarily affected by the disease. The author's hypothesis that the physiologic mechanism is one of coronary insufficiency does not seem well founded.

The statement that scar tissue in the heart does not lead to electrocardiographic changes unless it has interrupted important pathways or has interfered with the nourishment of a part of the myocardium is certainly one which has not been substantiated by adequate pathologic studies and, as an unqualified statement, is very likely to be wrong. It is an interesting theory that broad, notched P waves may be caused by intra-auricular block, but such a theory cannot be accepted without more definite pathologic evidence than has ever been demonstrated. Other equally satisfactory theories as to the abnormal form of these aberrant P waves have previously been advanced.

The author refuses to accept the localization of bundle branch block which has been established as a result of recent animal and human experiments and the

study of precordial leads. In its place he suggests a classification based upon certain more or less striking features of the curves in question. This is regrettable, for it seems that the localization of the site of bundle branch block has been established in a manner satisfactory to the majority of cardiologists. The fundamental points of distinction between the curves of right and left bundle branch block seem well enough established at present to warrant universal adoption, making such analyses of the records as suggested by the author totally unnecessary.

The sections on muscle physiology and anatomy are excellent in many respects, but it is regrettable that so often the individual opinion of the author is expressed without mention of the fact that it differs from that which is generally accepted. There is an interesting series of electrocardiograms on normal infants and young children, showing the progressive changes that may be found with increasing age. The numerous illustrations of the progressive effect of digitalis upon the T wave afford an excellent opportunity to study this feature.

The section devoted to the description of the changes associated with myocardial infarction and the healing which follows is one of the best parts of the book. The illustrations are numerous and give a complete picture of the development of the S-T and T-wave changes. Forty-four figures indicate the progressive changes in serial electrocardiograms taken over varying periods of time both before and after cardiac infarction. One can heartily agree with the author in his statement that the commonest error in electrocardiographic interpretations is the belief that the electrocardiogram can show the extent of myocardial damage.

There is an excellent and complete section on the cardiac arrhythmias. The author, as is usual, introduces a number of new terms and new subdivisions of old categories. In these instances the subdivisions seem to have a clearly definable basis and may be found helpful for more general use. It is doubtful whether the distinction between coarse and fine auricular fibrillation is of much importance, but, if it is important, a definite dividing line should have been suggested.

The chief value of the book to the beginner lies in the large number of illustrations and descriptive text. The difficulty for the beginner lies in the necessity of learning a large number of new terms, which he probably will not encounter in the vocabulary of other authors, and in the confusion resulting from the discarding or superseding of many commonly accepted definitions. The large number of illustrations are also valuable to the more advanced student who may wish to find records of certain rare conditions. The illustrations of electrical alternans will be particularly interesting to such a reader.

HAROLD E. B. PARDEE.

EXERCISES IN ELECTROCARDIOGRAPHIC INTERPRETATION: By Louis N. Katz, M.D., Director of Cardiovascular Research, Michael Reese Hospital, and Assistant Professor of Physiology, University of Chicago. Lea and Febiger, Philadelphia, 1941, 222 pages, 128 illustrations, \$5.00.

This volume affords an opportunity to review a large number of electrocardiograms in connection with certain salient features of the clinical conditions which have been selected by the author. Accompanying each record there is first a description of the individual features of the record, secondly, an interpretation of these features in terms of heart muscle physiology and pathology, thirdly, a brief picture of the patient's symptomatology and diagnosis, and, finally, what is called a correlation, which is a discussion of the contributions of the electrocardiographic record to an understanding of the clinical picture. It would be necessary for one to have previously read the parent book, because the author's terminology, which differs from that commonly accepted, is used throughout. One would not know,

for instance, the meaning of "left ventricular preponderance of the first type" nor the meaning of "a QRS of the Q type." Having mastered the author's terminology, however, there will be much to learn from a perusal of these records and the accompanying text for one who has not had much experience in interpreting electrocardiograms.

HAROLD E. B. PARDEE.

CLINICAL CARDIOLOGY, WITH SPECIAL REFERENCE TO BEDSIDE DIAGNOSIS: By William Dressler. Paul B. Hoeber Inc., New York, 1942, 692 pages, 108 illustrations.

This is a well-arranged, readable, complete book and the illustrations are well chosen. It is a clear, concise, ex-cathedra exposition of clinical cardiology. Throughout, the author has accepted the newest viewpoints. This is especially noticeable in his discussion of the pathogenesis of hypertension, of the natural history of rheumatic infections, and of the etiology of aortic stenosis.

The book has a very certain, but by the same token limited, appeal, in that it is written for senior students, young graduates, and general practitioners, especially for use during a post-graduate course. It is too advanced for younger students and too elementary for advanced students. It fails to point out and discuss the various aspects of the many problems which still await solution, and, above all, the author has chosen to omit all references to the literature. This is the worst aspect of the book, for every student should, as early as possible, be encouraged to seek the source records for himself. By this omission also the field of cardiological history is completely ignored. The modern cardiologist might find that the author overemphasizes physical diagnosis to the detriment of the newer, modern means of diagnosis; the electrocardiograph and the fluoroscope are no longer special instruments, but aids in physical diagnosis as indispensable as the stethoscope and the sphygmomanometer.

One must decidedly disagree with the author when he says (p.VI) that evaluation of electrocardiographic data has done more harm than good; when that happens it is due to poor judgment, and the complaint might, with the same justification (or lack of it), be lodged against stethoscopy or physical diagnosis; think of the interpretations given to "murmurs."

The reviewer also believes that the student for whom this book is meant would like to know, at least briefly, what kymography, phonocardiography, and other modern methods are and what they contribute, even though they are not of fundamental importance.

The ex-cathedra method of exposition has led to a number of statements which represent the author's opinion rather than what is generally accepted. Many of his views on myocardial infarction differ from those of other authorities; he fails to recognize "degenerative heart disease" as an etiological group comparable to infectious heart disease, and his use of the term "angina pectoris" is particularly distressing, in that he does not clearly distinguish between the pain of transitory anoxemia and that of myocardial infarction as suggested by the "nomenclature" (New York Heart Association), but he calls all pain from myocardial ischemia, angina pectoris.

A number of statements which appear so new and unusual are made without quoting his authority. Some seem to be suspended in thin air; for instance, when he says that about 50 per cent of the extrasystoles accompany organic heart disease (p. 235), it is necessary to state whether he obtained his statistics from a recruiting office, an office practice, or a hospital ward.

Of frank omissions there are not many beyond what may be expected by the limitation of the scope of the book. There are, however, some facts missing which should not be omitted even from an elementary textbook. The author does not mention xanthopia as a sign of overdigitalization; Wenckebach's periods, once mentioned, should be explained; the early combination of digitalis and diuretics in congestive failure. The figure giving the incidence of positive serologic reactions in syphilitic heart disease is not in the book. The importance of venous pressure measurements in the evaluation of cardiac function is not duly emphasized; the discussion of cardiac aneurysm can be found only by a thorough perusal of the text—it should be included in the index. There is no mention of the symptomatic effects of sympathectomy in hypertension, which, though difficult to explain, are real enough to be included in the effects of the operation. These are, after all, minor defects in an excellent book. Outweighing these criticisms is the fact that students were more than usually attracted to the volume.

On the whole, the book is a contribution to our didactic cardiological literature and should prove popular with the readers for whom it is meant.

JULIUS JENSEN.

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The Section for the Study of the Peripheral Circulation was organized in 1935 for the purpose of stimulating interest in investigation of all types of diseases of the blood and lymph vessels and of problems concerning the circulation of blood and lymph. Any physician or investigator may become a member of the section after election to the American Heart Association and payment of dues to that organization.

The income from membership and donations provides the sole financial support of the Association. Lack of adequate funds seriously hampers more intensive educational activity and the support of important investigative work.

Annual membership is \$5.00. Journal membership at \$11.00 includes a year's subscription to the AMERICAN HEART JOURNAL (January-December) and annual membership in the Association. The Journal alone is \$10.00 per year.

The Association earnestly solicits your support and suggestions for its work. Membership application blanks will be sent on request. Donations will be gratefully received and promptly acknowledged.

\**Executive Committee.*